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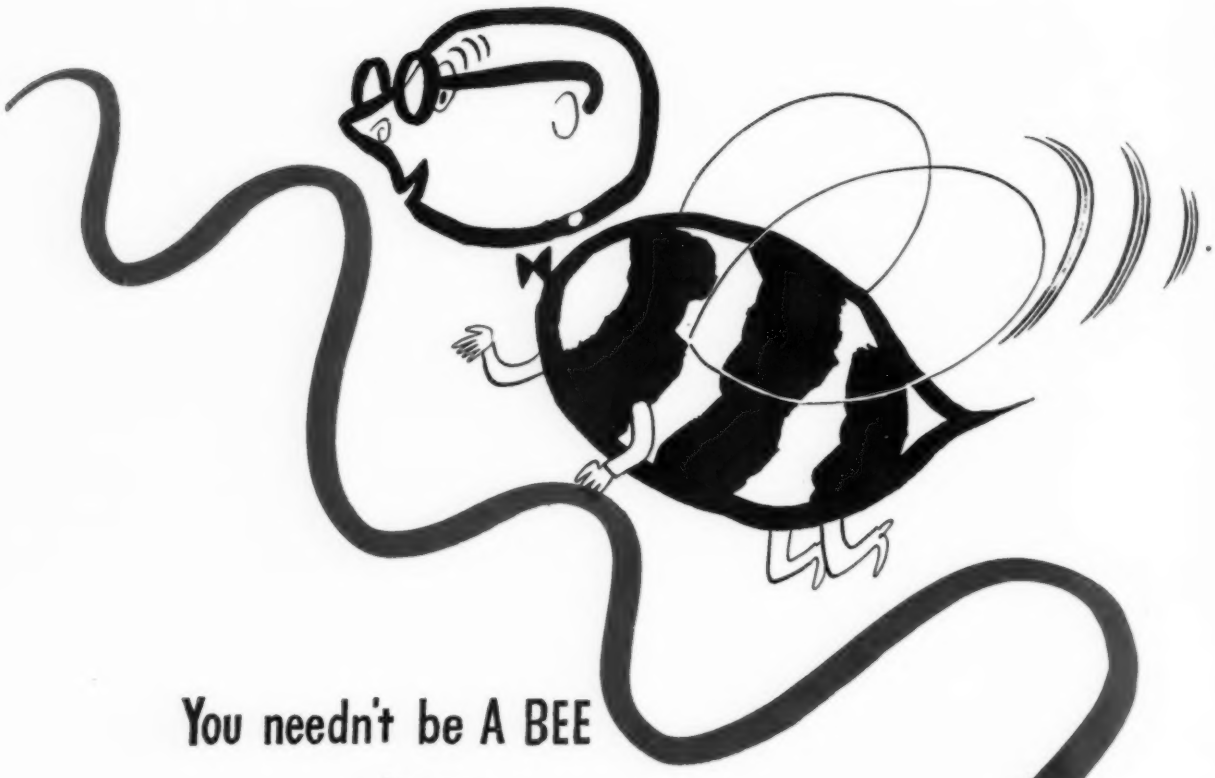
Drug and Cosmetic Industry

NOVEMBER 1954



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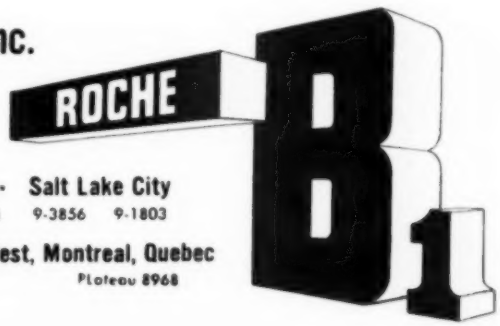

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Reprints of cover illustrations are available on request.

The Drug and Cosmetic Industry is published monthly by Drug Markets, Inc., Frazer V. Sinclair, President and Treasurer, Thomas R. Farrell, Vice-president and Secretary. Publication Address, 28 Renne Ave., Pittsfield, Mass., U. S. A. Editorial and General Office, 101 West 31st St., New York 1, N. Y., U. S. A.

Business Manager, Frazer V. Sinclair; Advertising Manager, P. W. Alexander; Advertising Representatives, Walter M. Brauneiss, C. R. Keeley; Production Manager, Katherine Hyde; Circulation Manager, Harry G. Kelbly.

Midwestern Advertising Representative: Dwight Early and Sons, 100 No. LaSalle St., Chicago 2, Telephone, CEntral 6-2184.

Subscription price $3.00 a year, in advance Foreign Countries, $5.00. Single copies, 35c; Back issues 50c. Entered as Second Class Matter, January 1, 1928 at the Post Office at Pittsfield, Mass., under the Act of March 3, 1879. Member of Audit Bureau of Circulations.

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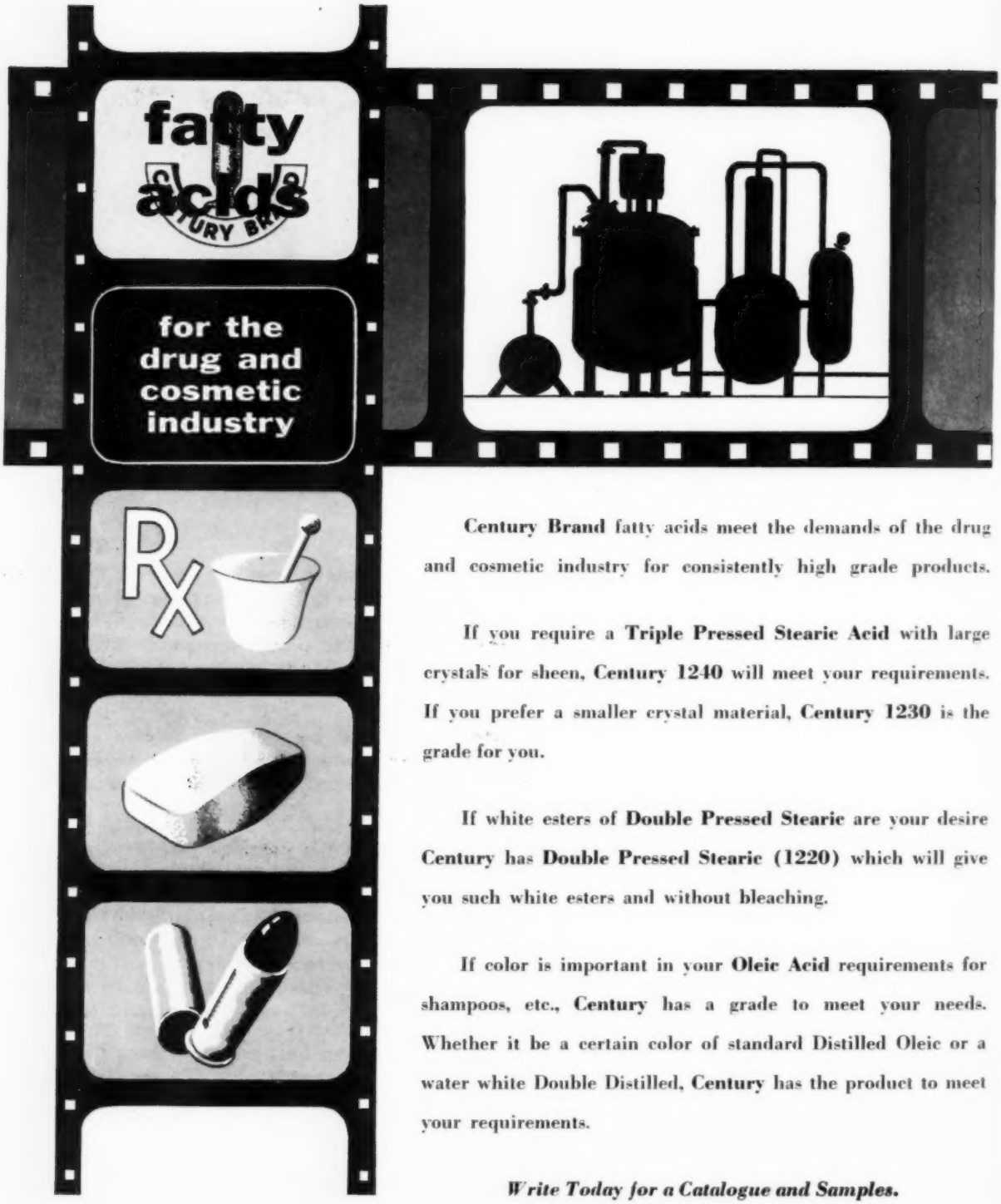

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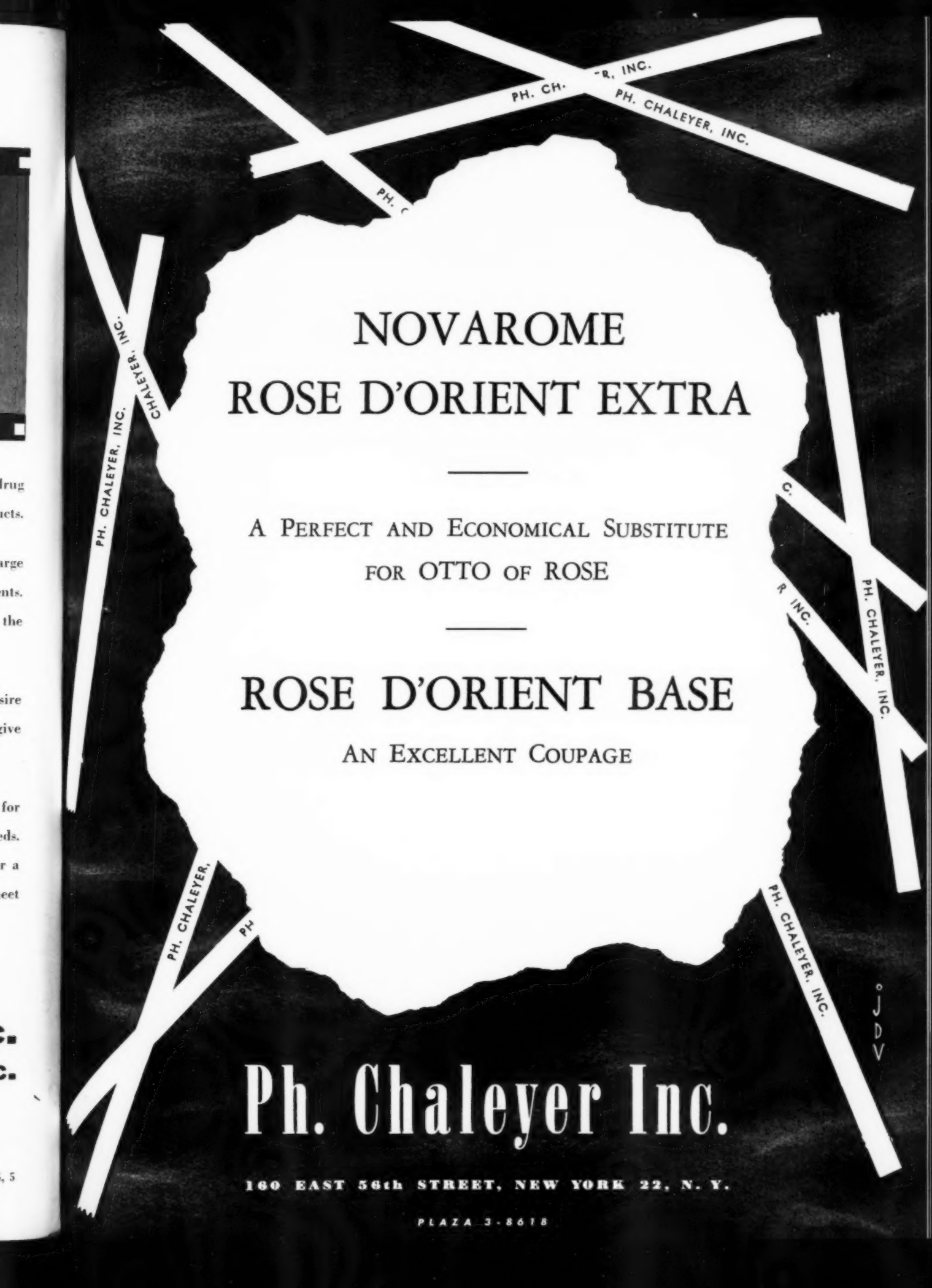

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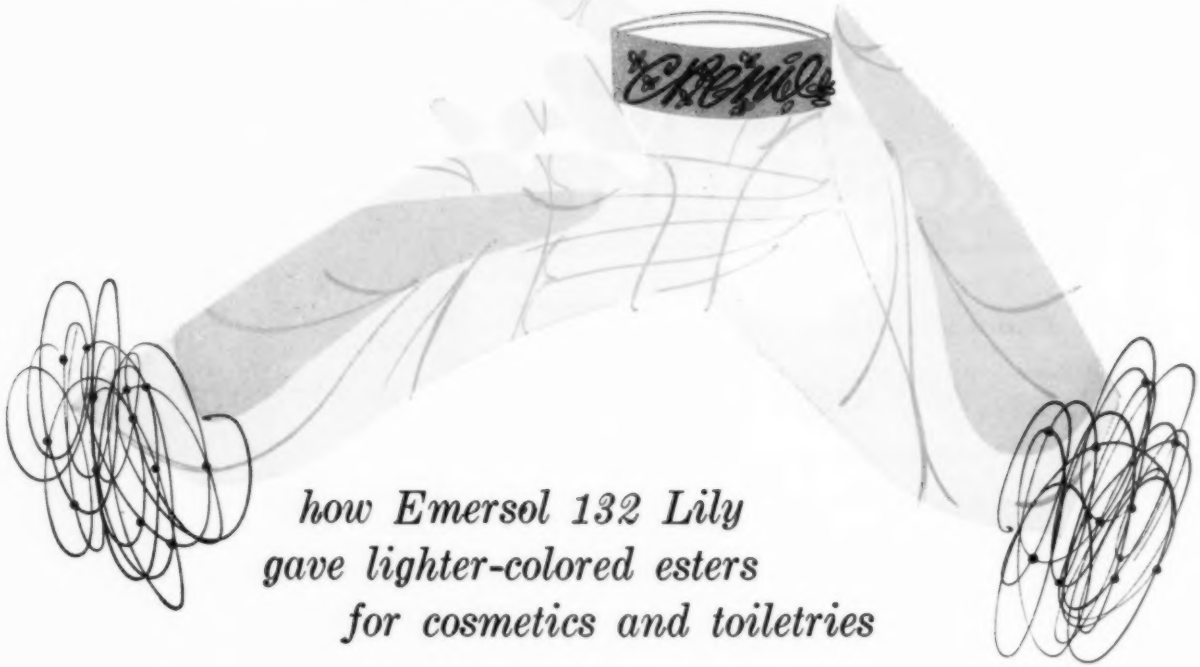

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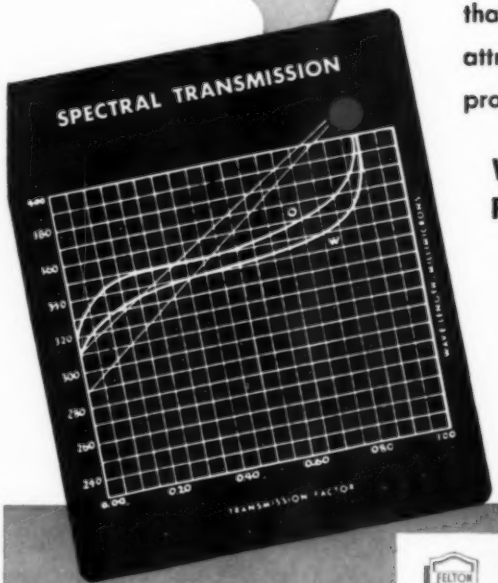

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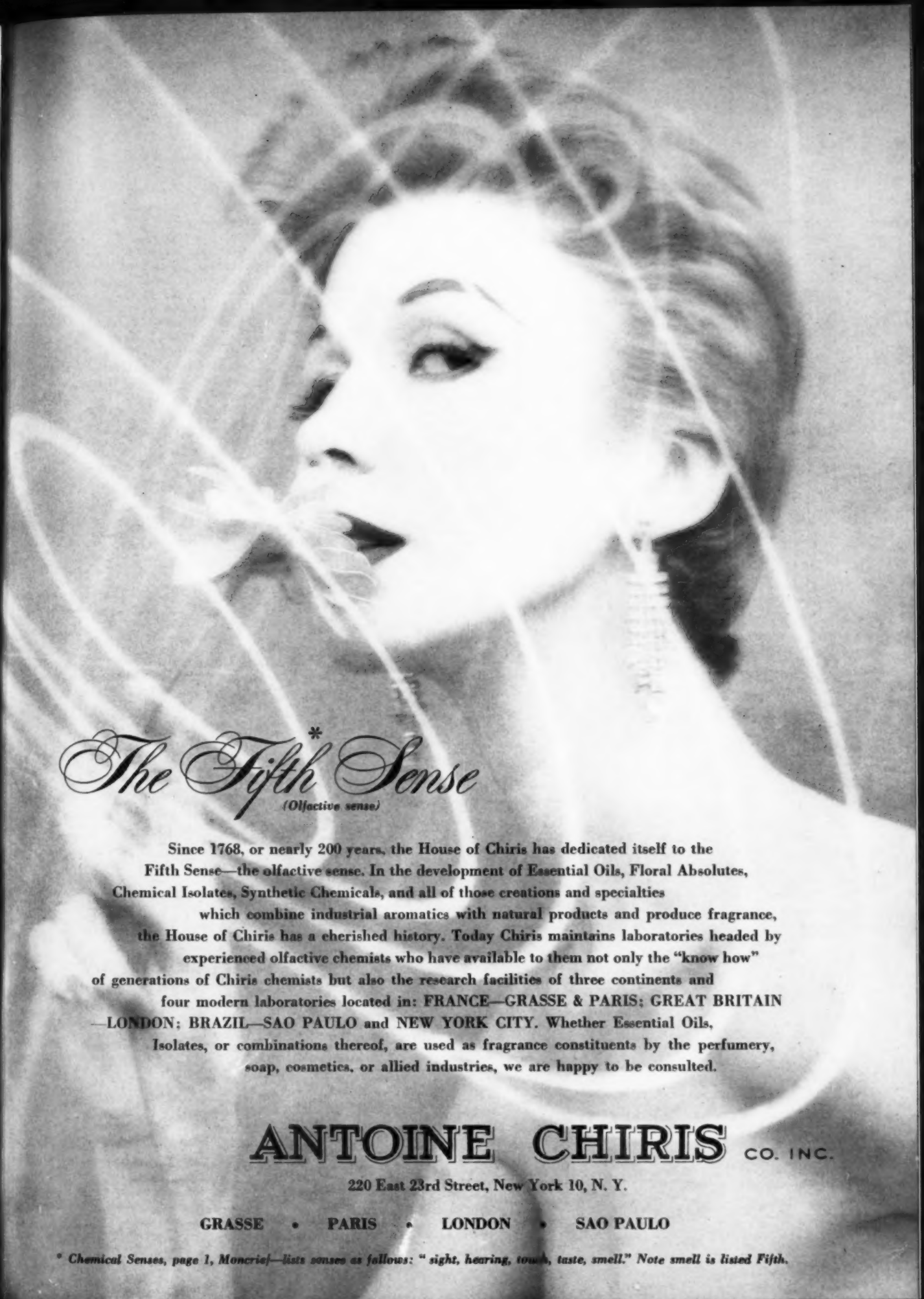

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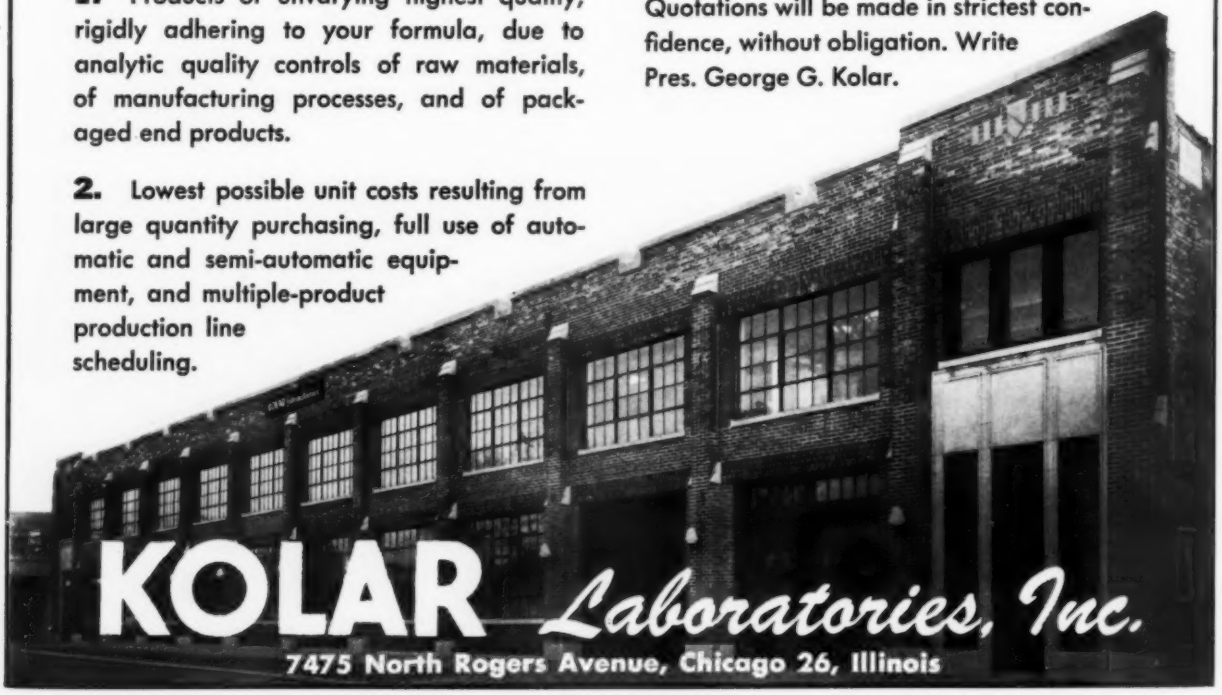

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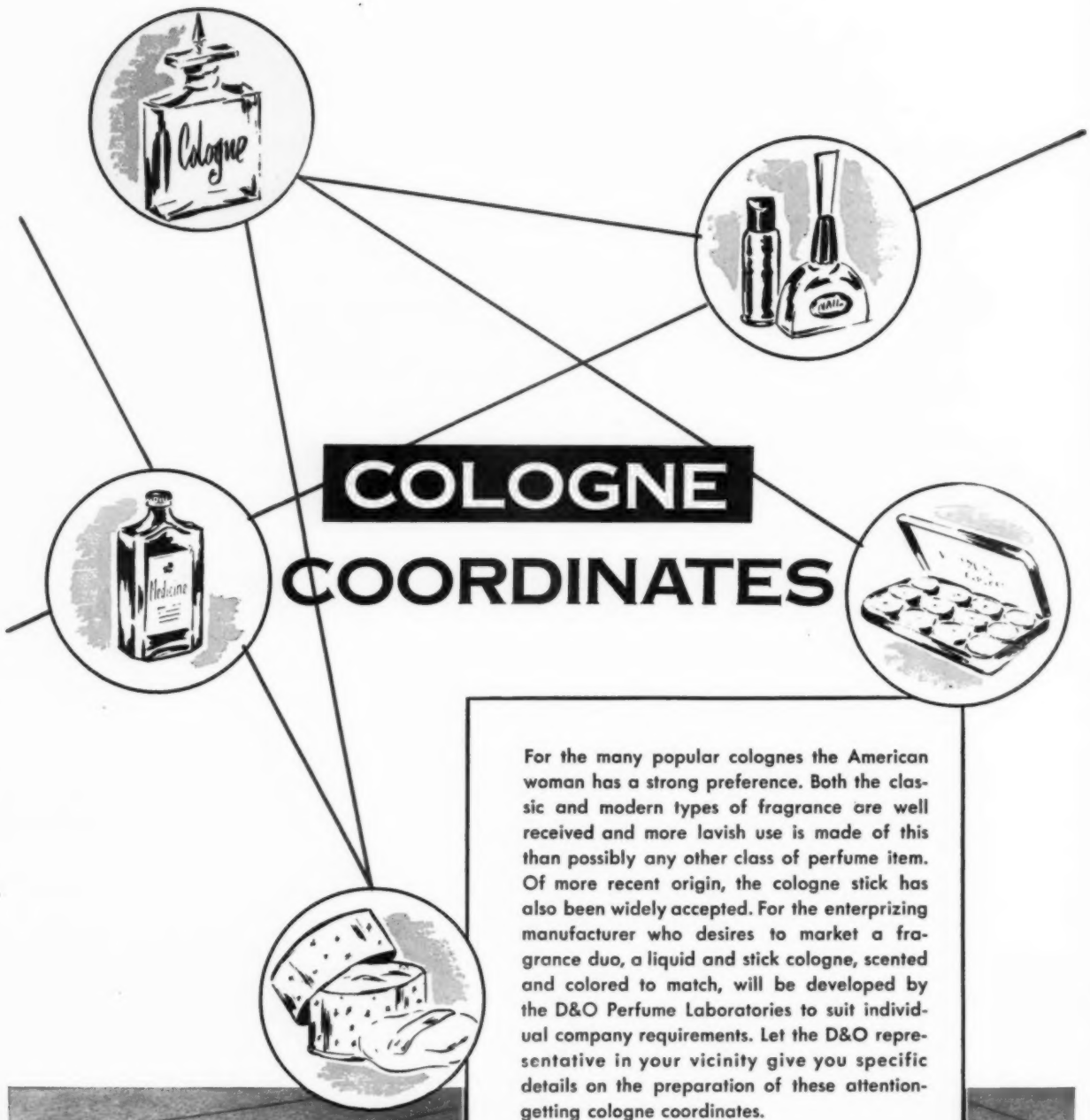

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6 They can be blended to make emulsions stable to freezing.

7 They enable you to make creams which, even after losing water, remain smooth, homogeneous and crust-free.

8 They are non-irritating to the skin.

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You will find valuable data on the use of these materials in the booklet, "A Guide to Cosmetic and Pharmaceutical Formulation with Atlas Products." Write for a copy today, using your company letterhead.

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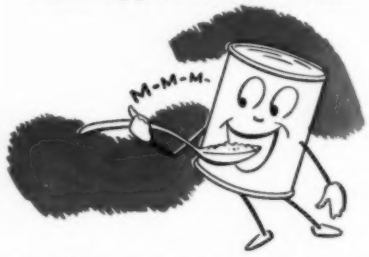

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A	Hystrene T-70 fatty acid. .	18.0%
	Mineral oil.	2.0%
	Lanolin	0.5%
	Arlacel 83	2.0%
B	Potassium hydroxide. . . .	0.7%
	Sorbo	3.7%
	Water	73.1%
	Preservative	q.s
C	Perfume	q.s

Preparation: Heat (A) to 90°C. Heat (B) to 95°C. Add (B) to (A) with stirring. Stir to 60°C., perfume and pour.

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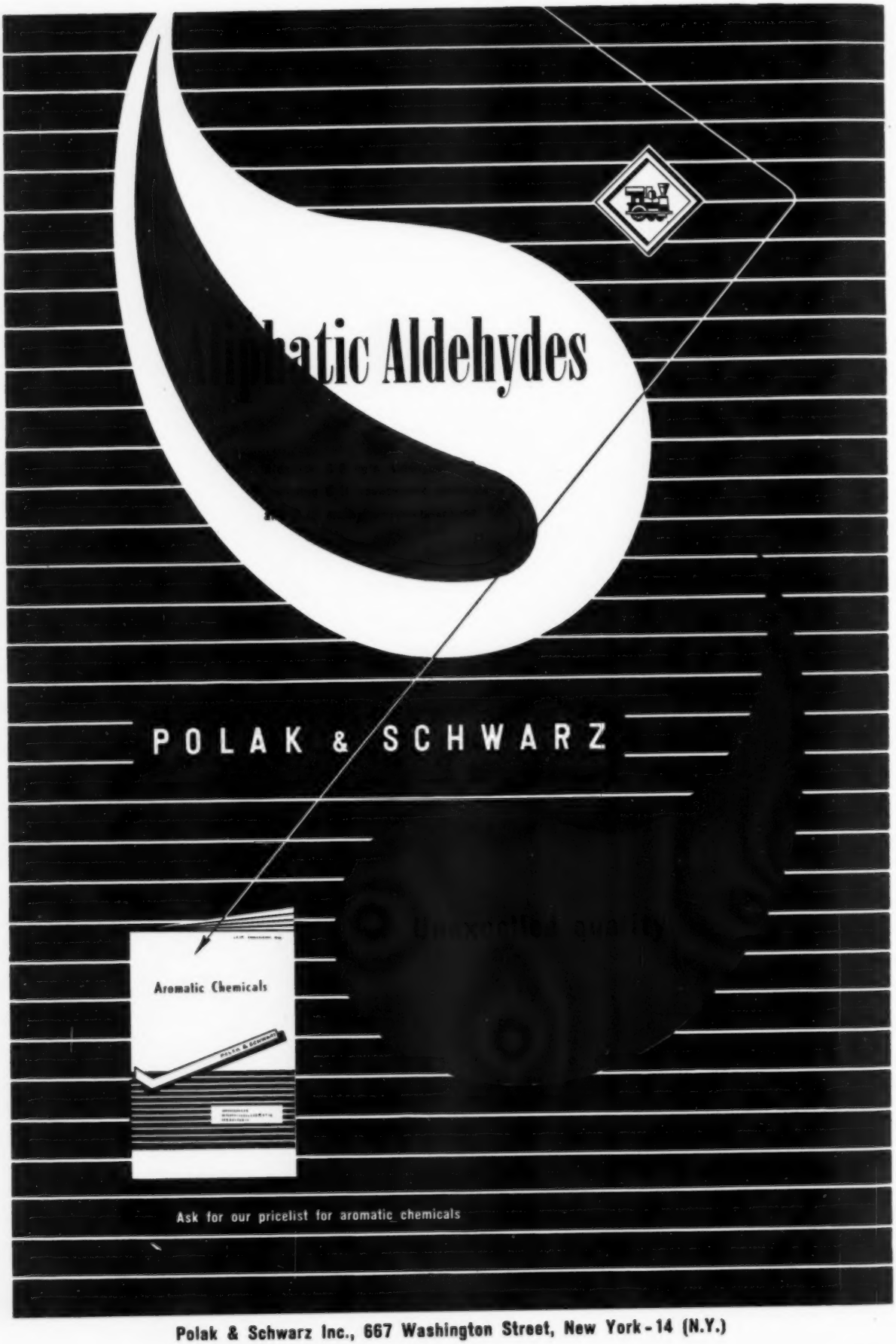

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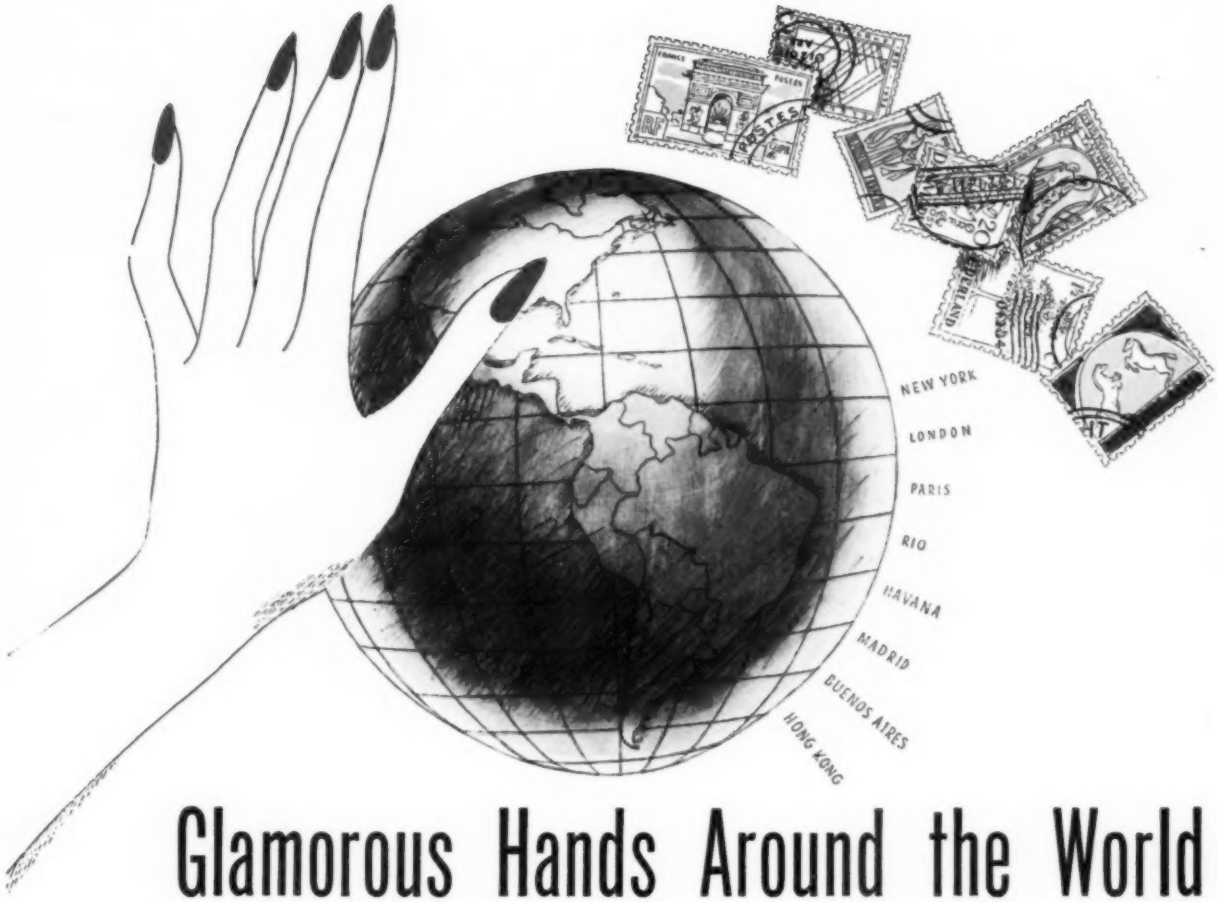

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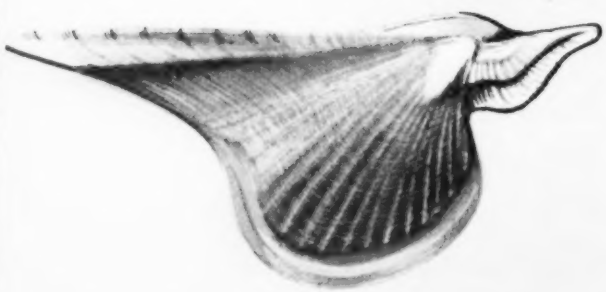

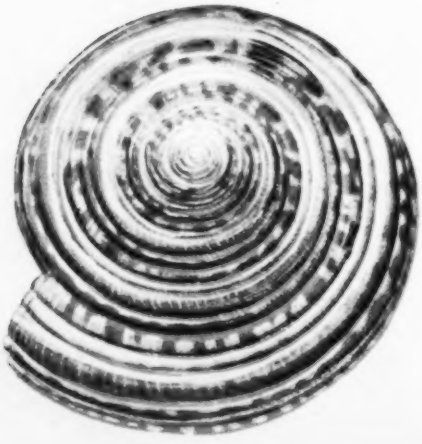

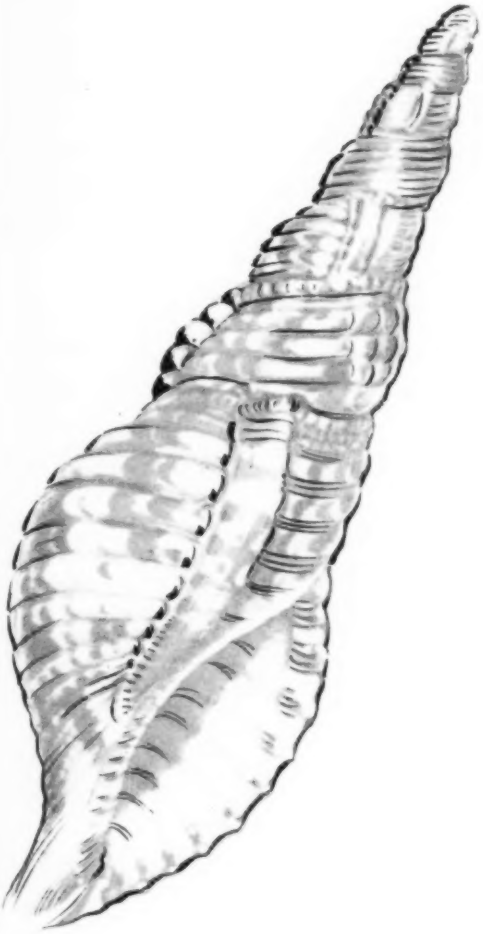

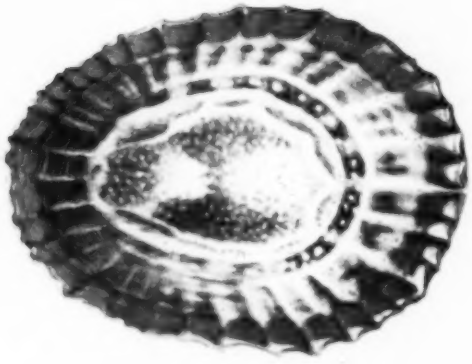

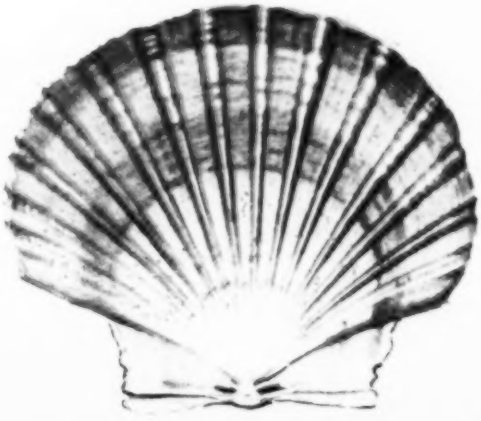

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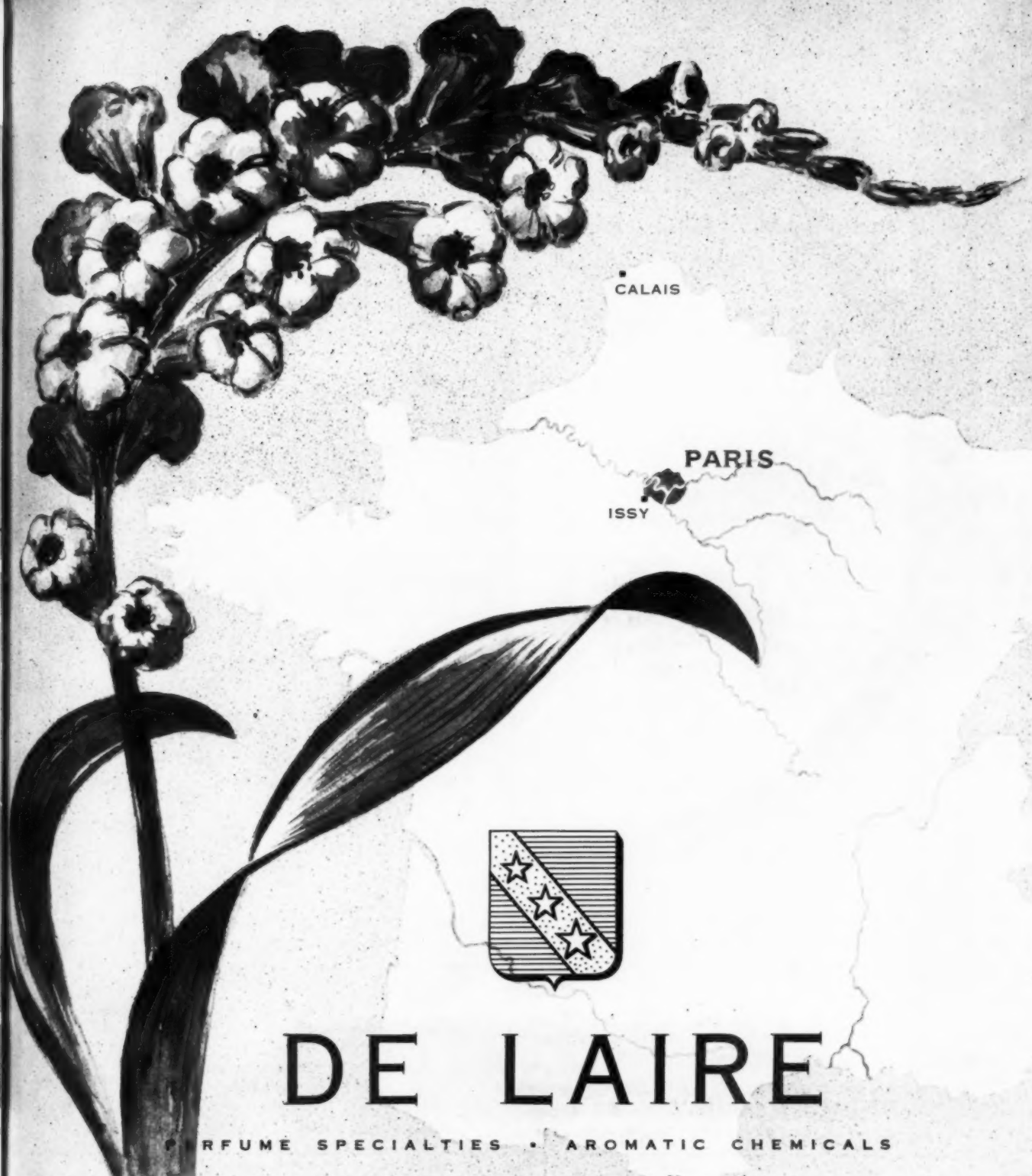

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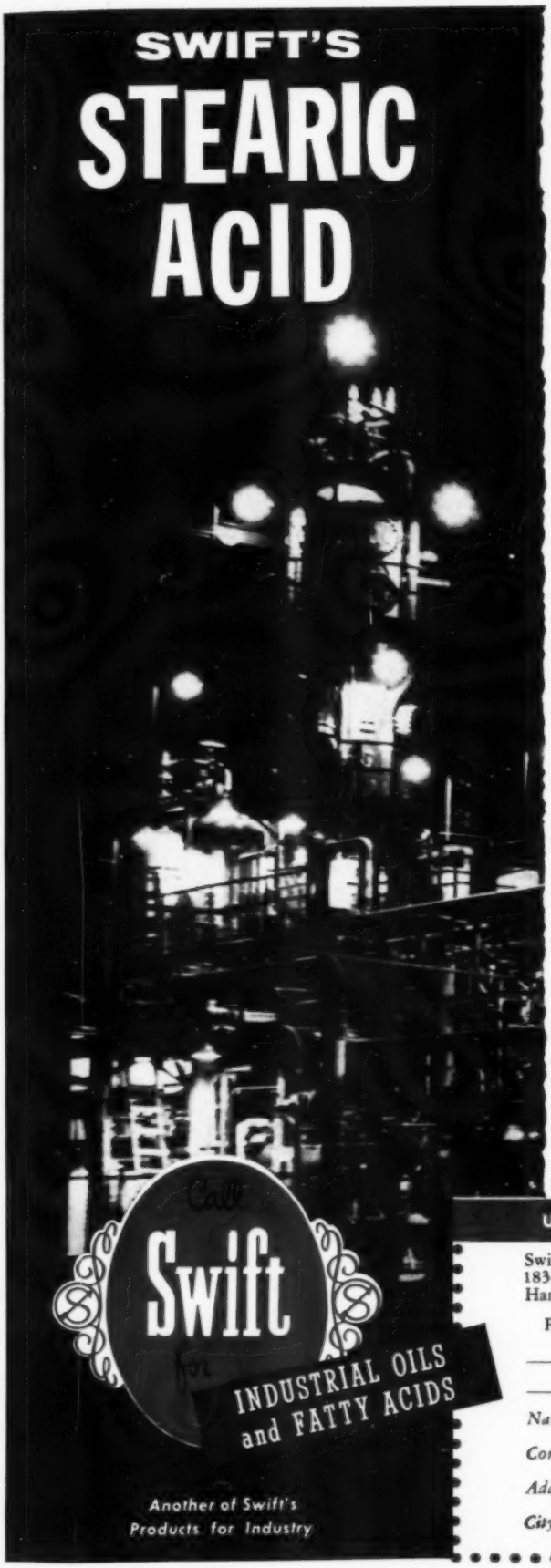

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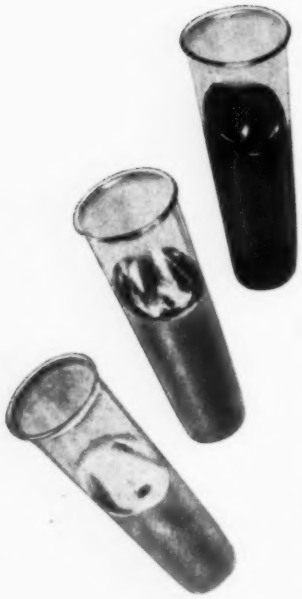

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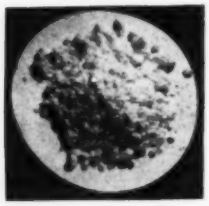

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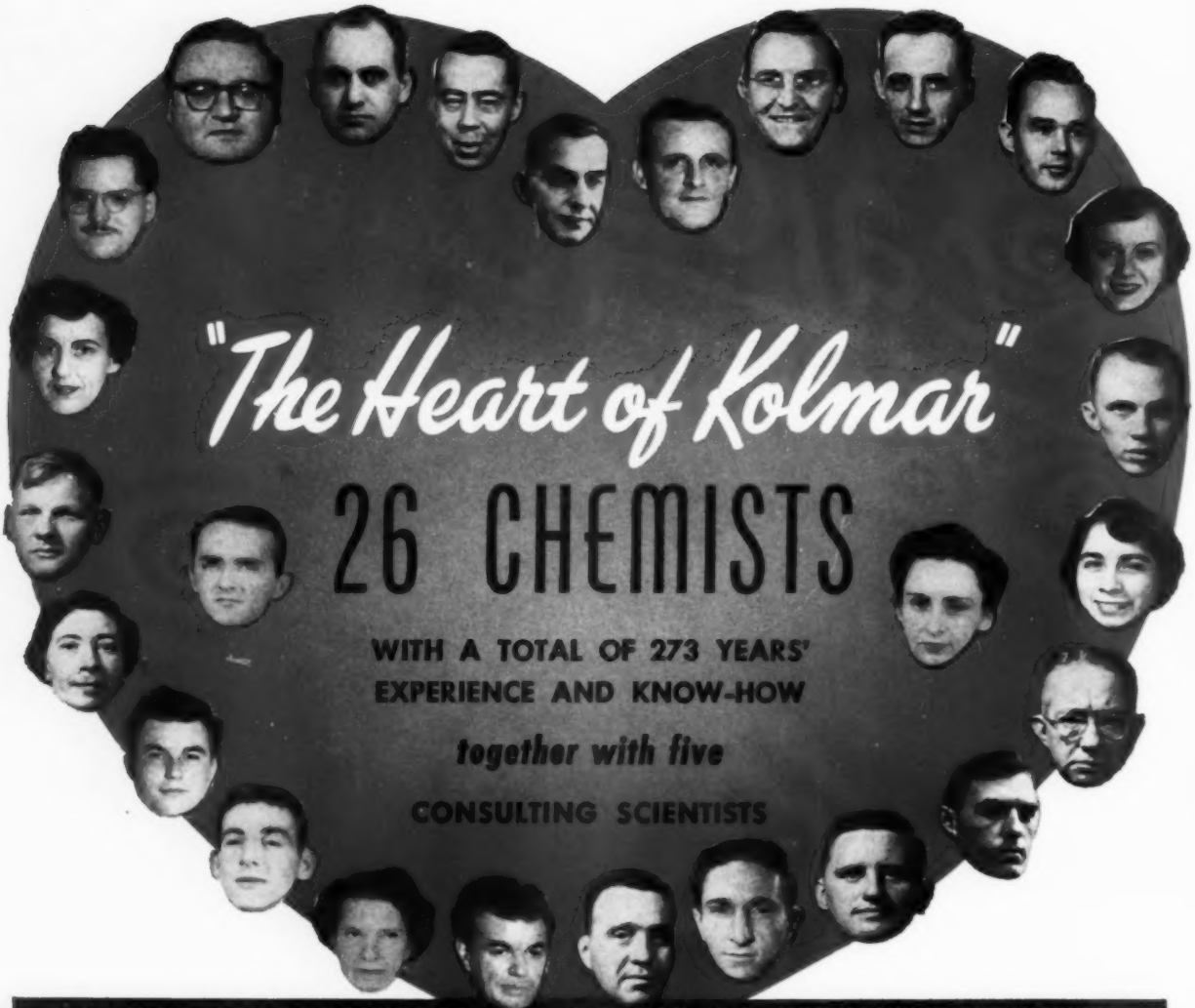
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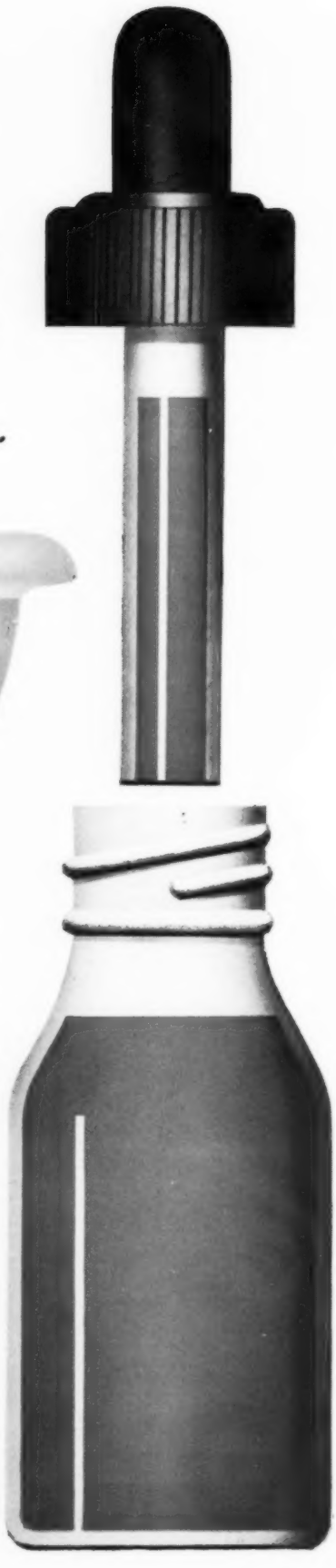

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Keeping Posted

Bristol Loses Tetracycline Interference

The U. S. Patent Office finally made a ruling in the long-standing controversy over the broad spectrum antibiotic, tetracyline. On October 13, the Patent Office granted the motions of Chas. Pfizer & Co. to exclude Bristol Laboratories and American Cyanamid Company (Lederle Laboratories) from the interference. The immediate effect of this decision is to leave Pfizer as the only company currently in a favorable position to obtain a patent on tetracycline.

The issuance of a patent to Pfizer would mean that no one would be allowed to produce tetracycline except Pfizer and Lederle, the latter firm having the right to the Pfizer patent through a cross-licensing agreement. Also Lederle owns the patent on chlorotetracycline (Aureomycin) from which tetracycline is produced.

Bristol Laboratories has recently been selling tetracycline hydrochloride to both Squibb and Upjohn. However, shortly after Bristol had put these two important pharmaceutical firms into the tetracycline business, Lederle sued Bristol under its 1949 chlorotetracycline (Aureomycin) patent, claiming infringement. The charge was that in its process for tetracycline, Bristol was producing chlorotetracycline. However, Bristol claimed that it had a fermentation process for production of tetracycline and denied infringement of the Lederle patent. It is stated by people who pretend to know, that it is impossible to produce tetracycline by fermentation without obtaining chlorotetracycline unless the process is kept chlorine-free, and this cannot be done.

However, now that Bristol's interference in its claim for tetracycline hydrochloride has been set aside, it seems that the Lederle suit against Bristol may not come to trial. For if Pfizer shortly obtains a patent, then the issue will be settled once and for all.

New Products and Merck

Nimbleness in developing new products will govern to a large extent the future success of Merck & Co., four executives of the company predicted last month at the fall manufacturing conference of the American Management Association. Speakers from Merck were Blythe M. Reynolds, vice-president for operations; Karl Pfister III, director, process research department; Frank L. Cohen, director of production; and Frank M. Parker, marketing director, Chemical Division.

Over the past two decades, said Mr. Reynolds, the growth of Merck has "to an unusual degree" resulted from the development of new products rather than from expansion of sales for products already in the line. In the Chemical Division, for example, more than two-thirds of profits come from products developed within the past twenty years.

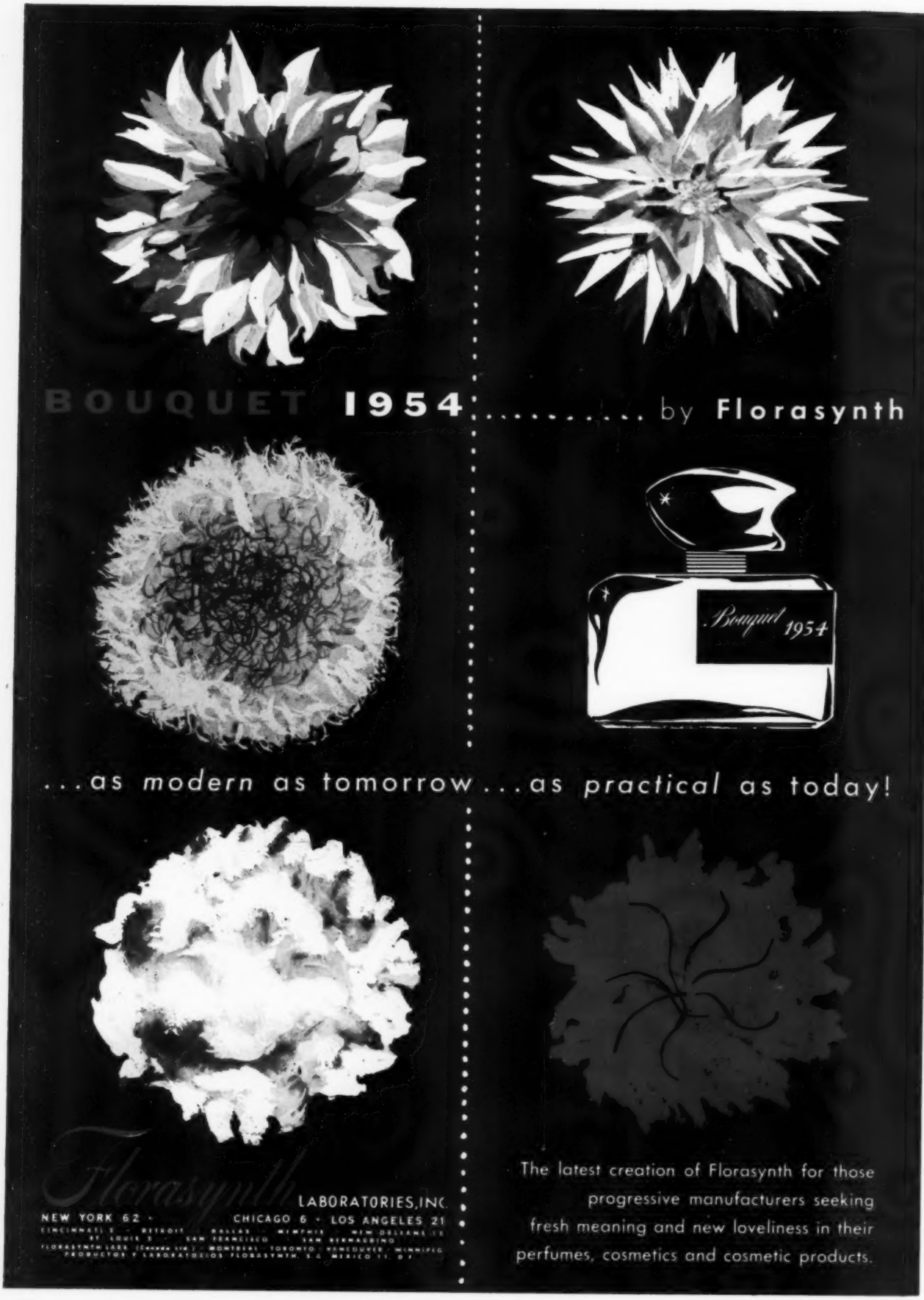
Development of a new product, according to Mr. Pfister, has two halves—to get hold of something that seems likely to turn into a valuable product and then to do something about it. The second part is more susceptible to management and control.

Getting the prospective product is primarily the responsibility of the exploratory research division, where most products make their start; however, ideas may come from other divisions of the scientific area as well as from marketing, production, or outside investigators and collaborators.

Even to colloraborate effectively with men in many fields, Mr. Pfister pointed out, requires broad experience and capability or flexibility within the company. Essentials are a broad exploratory program, including both chemically and biologically trained people, and determined maintenance of an atmosphere of receptivity to new concepts.

When a product is once established as a real possibility, the problems have only begun. "First, there is the shock of having one program, frequently not your favorite one at all, suddenly become the big job. Second, the need for speed. Finally, there is the frequent complexity of process with the corresponding need for large programs and heavy capital outlay."

The keynote of the exploratory program is breadth and diversification; with an actual product to develop, the aim is concentration of effort. "Sometimes," said Mr. Pfister, "I think we may overdo it. However, it seems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to us that at this stage of the game the dangers of underemphasis are far greater and infinitely easier to slip into than are those of overconcentration."

To coordinate this effort there is a scientific operations committee. Its work is supplemented by the new product steering committee, directly responsible for product development in the scientific area, whose duties are to evaluate and re-evaluate, determine the steps necessary for further development and assign work accordingly, set schedules, and follow up. An ad hoc group appointed by one of these committees at the laboratory or department-head level follows a particular potential product on a day-to-day or week-to-week basis.

Complete freedom of thought and action by all concerned and the teamwork developed through experience have contributed materially to Merck's new product developments, said Mr. Cohen. When a product has advanced far enough to warrant process development, both engineering and production personnel development are assigned to it. Process development is usually "an extremely complicated and sometimes confusing operation." The pattern involves streamlining of the process to make it satisfactory for factory operation; studies on recoveries, by-products, and waste disposal, "frequently tougher nuts to crack than the chemical processes involved in the new project;" supply; and costs.

In the project development stage design, safety, industrial, and chemical engineers take over. Flow diagrams, floor plans, engineering design, and building and construction requirements are worked up, and a final capital estimate for the project is prepared. Unfortunately, said Mr. Cohen, the research people are not idle between the process development stage and preparation for the process break-in. Sometimes they succeed in eliminating steps in the operation or substituting cheaper or better raw materials; then revised capital estimate must be made.

"It is not at all uncommon that specially designed equipment is obsolete before fabrication is completed. By the same token, building requirements are sometimes changed before the concrete and mortar are dry." Even after a process has started running smoothly, it is taken over by a new group of development chemists who trouble-shoot it, mother it, and invariably improve and modernize it many times in the course of its life in the plant. Process development is never finished. Break-in of the new process is again a teamwork proposition, concluded Mr. Cohen. "Invariably the break-in goes quite smoothly, which attests to the fine workmanlike job done by everyone concerned." Once yields, capacities, quality of products, and recoveries are satisfactory and the necessary safety requirements are met, a new product is ready for distribution and sale.

The marketing department participates constantly in every research project from its beginning, reported Mr. Parker. As a result "we endeavor to have the complete marketing program in high gear and ready to start coincident with initial inventory availability." Another Merck philosophy is that the marketing department, through its market analysis section, determines production requirements, and the production units at all plants produce these requirements without second guessing on sales needs. This is also true of new-product planning. While interlocking of the marketing people with research sometimes results in duplication of effort, such duplication is justified to keep changes in product and plans to a minimum after actual selling is under way, said Mr. Parker.

Because of the highly technical nature of the products and the frequency with which products change, the marketing department puts heavy emphasis on technical qualifications. Marketing department personnel are 76 per cent technically trained, many of them with advanced degrees.

Today it is frequently true, Mr. Parker concluded, that marginal advantages alone effect success in selling since the competitive race is keen. "New products, product improvements, quality advantages, nimbleness to market, good forecasting, well-planned and adequate selling, effective promotional support, adequate technical foundations, low costs and, last but not least, enthusiastic teamwork among research, marketing, and production tend to produce advantages."

Conditions

H. P. Weseman, first vice-president of Fritzsche Brothers, recently returned from a six-week trip to England, France, Germany, Austria, Italy, Switzerland, and Spain, while professing only amateur standing as an economist, states he was most favorably impressed with the business outlook in England, Germany, and Spain. England's economy is on the way up, he said, and as soon as her currency is again free, she will be ready once more to resume her position as the outstanding center of world trade. One favorable aspect of an otherwise heavy tax burden is the fact that England has no capital gains tax, which is helpful to those who can take advantage of it, he pointed out. Twenty-five thousand dollars is the top limit any individual can retain from earnings and, even at low levels, the tax is excessive. But in spite of this the people are quite content.

In France business opportunities have been curtailed, unfortunately, by government controls of financing in connection with the licensing of imports.

Weather conditions in Spain have been generally unfavorable for products for the essential oil industry and almost all prices have advanced as a result. However, the country itself is making rapid strides, due principally to U.S. aid which is everywhere acknowledged as contributing materially to a growing middle class—in the past Spain's greatest lack, and today her greatest need, if good times and a healthy economy are to prevail.

In Western Germany, the business outlook is extremely hopeful. There is tremendous activity and much competition throughout the nation. The influx of refugees from East Germany—many of whom arrive with little money and a desperate need for some means of livelihood—has contributed to this very competitive situation. Everyone is trying to make a living and ready to accept a minimum of profit to make sales. Quality is no longer of much concern to anyone. The average wage for skilled labor is around $15 per week. Good coffee sells for about $3.50 per pound, but such high-priced items are offset by quite low prices for other commodities.

Mr. Weseman spent much of his time with various producers and exporters of basic raw materials. He covered essential producing areas in both Spain and the

PHARMACEUTICAL

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eastern Tyrol and was able to verify, at first hand, the conditions responsible for current prices of the oils originating in these countries. He observed that the identical factors—weather and labor—that affect the availability of oils produced in Pennsylvania, Indiana, or California, are responsible for the supply and prices of oils produced abroad. Even with labor averaging only 80 cents a day in Spain, the scanty supply of oils produced in drought-ridden areas of that country bring much higher prices than when favorable weather creates lush supplies.

Mr. Weseman noted that many aspects of the European picture are more favorable than we in this country believe, and he expressed assurances that America's contributions to Europe's advancing economy are not wholly unappreciated.

Loynd Honored in Colorado

Harry J. Loynd, president of Parke, Davis & Company, was recently honored by a group of Coloradoans, headed by Governor Dan Thornton. The Governor presented the state's Certificate of Merit to Mr. Loynd who came to Colorado with his parents when he was seven years old. He lived in Lamar, Rocky Ford and Manzanola and got his start in the retail drug business at Fowler, working a regular shift in a drug store outside school hours. Approximately 300 persons, including many prominent in government, medicine, and pharmaceuticals, attended the affair sponsored by the Pueblo Lions' Club in Colorado State Hospital.

Revlon Agreements Banned

Revlon can no longer have exclusive sales agreements with beauty supply jobbers, according to an order of the Federal Trade Commission in which the Commission denied Revlon's appeal from an initial decision of a hearing examiner. These agreements—made with 157 of the 176 very best jobbers Revlon sells in a field of 1,500 jobbers, of which 1,100 are good credit risks—contained the following provisions:

1. Nail enamel and related manicure products—jobbers required to deal in Revlon products exclusively.
2. Lipsticks, face powder, rouge, creams, lotions and other make-up cosmetic products—jobbers required to deal exclusively in Revlon products "except that they are permitted to deal in any of this class of products which are part of a competitor's complete make-up and treatment line."
3. Nail enamel remover—exclusive-dealing required "except the jobbers are allowed to sell competitors' nail enamel remover under the jobber's own brand or trade name."

While Revlon started its business by selling only to the beauty shop trade—first directly and then through jobbers—sales to the retail trade generally, both through jobbers and directly, eventually became the principal part of the business, accounting for over 80 per cent of total sales.

Revlon sells around 200 different cosmetic items, of which its largest selling products are lipsticks, nail enamels and allied manicure products. Revlon specializes in the more expensive nail enamels and polishes, in which field it is the leader and is dominant. Revlon is also a leading seller of lipsticks, which comprises its largest volume of business.

Revlon's sales through its beauty supply jobbers, in 1949, totaled approximately one and a half million dollars. Of these sales, over six hundred thousand dollars were of nail enamel and other related products listed in subdivision I of the franchise agreements, over eight hundred thousand dollars were of lipstick and other cosmetic products listed under subdivision II of the agreements, and the remainder consisted of sales of about sixty thousand dollars worth of nail enamel remover, the product listed in subdivision III.

FTC Cites Health Insurance

Seventeen insurance companies issuing policies in the billion-dollar hospitalization, accident and health insurance business are the subject of FTC complaints charging false and misleading advertising.

In the aggregate, the 17 companies account for annual premiums of over $300,000,000, representing about one-third of the total accident and health coverage on an individual policy basis in the United States. The four largest companies in this field—Mutual Benefit Health & Accident Association, of Omaha Nebr. (Mutual of Omaha); Bankers Life and Casualty Company, of Chicago (The White Cross Plan); Reserve Life Insurance Company, of Dallas, Texas; and United States Insurance Company, Chicago—are among the 17 companies cited for misrepresentation of their policies.

The legal proceedings follow a nation-wide investigation announced by the FTC ten months ago. The investigation grew out of a flood of letters received from American policy-holders complaining that the insurance coverage they purchased was not the coverage that had been advertised. The investigation is continuing.

The Commission points out that this field of insurance has had tremendous growth in recent years. Total 1953 premium payments for accident and health insurance amounted to more than three billion dollars. Of this total, over one billion dollars in annual premiums is received by companies selling policies on an individual, non-group basis, and here especially advertising is widely used, says the Commission.

This compares with premiums of $161,000,000 in 1935, and represents an increase of more than 200 per cent over 1946. Approximately 25 million persons have purchased individual policies. Twenty-five years ago, there were only 50 companies writing accident and health insurance, while today there are approximately 900 companies in the business.

In general, the proceedings are directed against the use of false or deceptive advertising claims relating to the extent of the coverage provided and the benefits payable under accident and health policies. The complaints allege the use in advertising of false representations, deceptive or misleading statements, and deceptive concealment or non-disclosure of exceptions and limitations.

Of the categories of false and misleading advertising with which the companies are charged, all seventeen of the companies were found to be falsely advertising the extent of coverage; fourteen were found to be misrepre-

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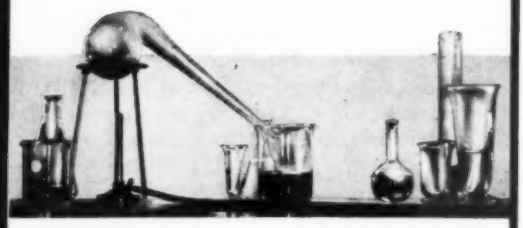

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PHARMACEUTICAL MANUFACTURERS TO THE TRADE - SINCE 1833

senting the termination of policy; eleven were misrepresenting the maximum dollar limits; eight were falsely claiming payment of benefits for life; seven were deceptive about the health status of the applicant; four misrepresented the sale of a plan; and three misrepresented the starting time of coverage.

In addition to the four companies named above, the following companies are cited: The American Hospital and Life Insurance Company, San Antonio, Texas; American Life and Accident Insurance Company, St. Louis; Automobile Owners Safety Insurance Company, Kansas City, Mo.; Commercial Travelers Insurance Company, Salt Lake City; The Commercial Travelers Mutual Accident Association of America, Utica, N. Y.; Guarantee Reserve Life Insurance Company of Hammond, Hammond, Ind.; Guarantee Trust Life Insurance Company, Chicago; Illinois Commercial Men's Association, Chicago; La Salle Casualty Company, Chicago; Life Insurance Company of America, Wilmington, Delaware; Prudence Life Insurance Company, Chicago; Southern National Insurance Company, Little Rock, Ark.; Travelers Health Association, Omaha, Nebr.

Pharmaceutical Sales Abroad

Pharmaceutical manufacturers of the United States are doing business abroad at an annual rate of approximately $250,000,000, or about 25 per cent of the total U. S. chemical export volume of almost one billion dollars, according to C. A. Specht, president of Pfizer International Subsidiaries. Correspondingly, American investments abroad in the chemical and pharmaceutical fields have shot up about 150 per cent since 1939 as compared with an increase of only 50 per cent in total U. S. foreign investments, said Mr. Specht, who added: "this phenomenal increase can be attributed in part to the fact that during the war, many foreign chemical plants were destroyed, or deteriorated, and research and development, under the pressure of war conditions abroad, lagged. In contrast, this country saw not only an expansion of its chemical production facilities but research and development received considerable impetus."

Works of Lavoisier

A Bibliography of the Works of Antoine Laurent Lavoisier 1743-1794, by Denis I. Duveen, Fellow of the Royal Institute of Chemistry of Great Britain and Northern Ireland, and Herbert S. Klickstein, Edgar Fahs Smith Library in the History of Chemistry, University of Pennsylvania, with a preface by John F. Fulton, Sterling Professor of Medicine, Yale University, has been published by Wm. Dawson & Sons, Ltd. and E. Weil, London.

Mr. Duveen, president of Duveen Soap Corporation, Long Island City, N. Y., is the world's outstanding authority on memorabilia of Lavoisier. The prospectus says:

"Based on the unique Lavoisier collection of Mr. Duveen, the joint authors, with the help of friends and librarians all over the world, have described and analyzed the work of Lavoisier, revealing his true stature as not only the great chemist, but as an agriculturist, physiologist, physicist, economist, meteorologist and last, but not least, a great administrator. Instead of the 60 papers usually ascribed to him, 120 are now listed. Of his four major works 70 different editions are meticulously described bibliographically as well as 32 minor works in 77 editions and well over 20 miscellaneous contributions of Lavoisier to the works of other authors. The contents of all these works are critically examined." The edition is limited to 750 copies of which 10 are on hand-made paper and not for sale.

Product Ingredient Dictionary

A dictionary which is expected to help save many of the 1,500 lives lost annually through accidental poisoning will be published within the next year by Dr. Harold C. Hodge, professor of pharmacology and toxicology at the University of Rochester School of Medicine and Dentistry, and Marion Gleason, a research associate. The book will be the first complete medical dictionary of trademarked and generally known products which might be involved in accidental poisoning in the home. The book will list products; their hazardous ingredients, if any; the degree of damage to be expected from swallowing them accidently, and what to do about it. Working on the project for over four years, the two scientists have collected and analyzed data on about 15,000 products which will form the bulk of the book's contents.

Squibb Chemical Division

Olin Mathieson Chemical Corporation has formed a new unit known as the Squibb Chemical Division to engage in the development and marketing of antibiotics for agricultural use, and specialized chemicals. Frederick J. Stock has been named general manager of the new division; Francis J. Reid has been named director of sales; and Dr. W. E. Bunney has been named technical director. Mr. Stock joined the Mathieson organization in 1952 following his retirement as vice-president in charge of sales of Chas. Pfizer & Co. that same year. Mr. Reid comes to Squibb Chemical from New York Quinine & Chemical Works of which he was executive vice-president. Dr. Bunney transfers to Squibb Chemical from the E. R. Squibb & Sons Division of Olin Mathieson Chemical Corporation with which he was associated for over sixteen years. Dr. Bunney joined E. R. Squibb & Sons in 1938 as director of biological products output.

Yeast- and Algae-Fed Animals

Yeast-fed or algae-fed animals will be part of the human diet within the foreseeable future because the world's population is increasing so fast that it will be necessary to double, or even triple, food production before the year 2,000, according to Dr. Ernest H. Volwiler, president of Abbott Laboratories and chairman of the board of the American Chemical Society. In his address following his reception of the Chemical Industry Medal of the Society of Chemical Industry "for

conspicuous services to applied chemistry," Dr. Volwiler said that hydrophonics—growing plants in vats containing minerals and nitrogen nutrients dissolved in water—appear to be too costly to relieve much of the world's food shortages.

"A more feasible procedure," he said, "would be to supply human food, particularly protein, through the growth and consumption of certain types of yeast or algae. This, however, would signify such a drastic change in food habits that it is more likely in the foreseeable future that such food sources may first be fed to animals which in turn will be consumed by man."

He pointed out that there will be a billion more people in the world by the year 2,000—46 years from now—if the rate of population increase does not change. "At the present rate of population increase, to which all continents are contributing," he said, "food production by the year 2000 should be increased two to three times over what it is today."

MCA Wins Safety Award

The Manufacturing Chemists Association has been selected for a 1954 National Safety Council Association Award. The Association Awards are made annually by the NSC to those trade associations who most actively promote safety in small business. In making these awards, the judges take into consideration accident prevention activities such as publicity, safety conferences, contests, and publication of technical material.

Last year the chemical industry ranked eighth in the 40 major industries in accident frequency rate. The comparable standing for companies in the MCA safety program was fifth. The chemical industry as a whole has shown an improvement of more than 50 per cent over its 1935-1939 average. For the first six months of 1954 the accident frequency rate of participating MCA companies was 65 per cent better than the NSC 1935-1939 average rate. The NSC industrial injury statistics are based on a broad cross section of 851 reporting units, while the MCA figures reflect the rates of its member firms.

24,000 Million People a Day

Twenty-four million people visit the country's 53,000 drug stores every day, according to Graydon L. Walker, director of sales and promotion for Parke, Davis & Company, who added: "The possibilities offered by this opportunity to elevate the status of pharmacy and influence the health and well-being of the nation are staggering."

"Here is a thought that startled me," said Mr. Walker. "We read of subversive organizations which exist in a twilight zone of activity because their objectives are not acceptable to the average good American. Suppose such an organization suddenly found that it had 53,000 units of contact with 24 million people a day—15 per cent of the population of the country every day of the year—and under the same conditions of trust and confidence which the 53,000 drug stores of the country enjoy today. Do you think they would underestimate the value of that opportunity?"

The "third dimension" of pharmacy is the relationship between the drug store and its customers, according to Mr. Walker.

"It is a fact," he emphasized, "that the most important thing in business is people—people in the act of buying or selling some commodity or service. Stated so simply, this seems over-obvious—yet this fundamental principle is often overlooked and sometimes completely ignored."

Hazel Bishop Facts

Hazel Bishop Inc. made a public offering of 250,000 shares of common stock late last month. The stock was sold at $8.00 a share for a total of $2,000,000. After underwriting discounts and commissions of $1.00 per share, the proceeds to the company for the 150,000 shares which it sold is $1,050,000; and Raymond Spector, chairman of the board and principal stockholder, for the 100,000 shares sold by him, $700,000.

Outstanding stock of the company after the sale was 1,088,000 shares of common stock, of $10.00 par value, and 84,420 shares of six per cent convertible preferred stock of $10.00 par value which is convertible into three shares of common stock for each share. After the sale, Mr. Spector was the holder of 388,500 shares of common stock constituting 35.71 per cent of such shares; and the combined holdings of Mr. Spector and Raymond Spector Company (of which Mr. Spector owns 76 per cent of the stock) are 51.65 per cent of such stock. Mr. Spector also owns 55.28 per cent of the preferred stock, and Raymond Spector owns 21.32 per cent of this stock.

Sales of the company totaled $8,313,185 for the nine months ended July 31, 1954. For the year ending October 31, 1953, sales totaled $9,908,804; for 1952, $4,549,165; for 1951, $2,814,546.

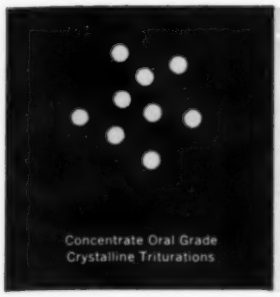
The company claims that it is doing approximately 25 per cent of the total lipstick business in this country, and that the company and its two major competitors account for approximately 50 per cent of the lipstick business.

The company also claims that Hazel Bishop Complexion Glow is the largest selling rouge in the United States, and that it accounts for approximately 50 per cent of the total dollar volume of sales. Other cosmetic companies have introduced liquid rouges, says the company, but the leadership of Hazel Bishop in this field has been maintained.

Hazel Bishop Long Lasting Nail Polish, retailing at 60 cents, against 25 cents or under for most brands, has achieved substantial consumer demand in the relatively short time since its introduction, it is claimed. Said to be doing approximately in dollar sales, 15 per cent of the total nail polish business in the United States, more aggressive promotion is to be initiated.

Until August, 1954, the company had all its products manufactured and shipped by others. However, the company has acquired a plant in Paramus, N. J., and is bottling a substantial portion of its Complexion Glow. Machinery has been ordered for bottling a substantial part of its nail polish and for manufacture of a substantial portion of its lipsticks.

In the near future, the company intends to establish bottling and shipping facilities in the midwest and on the west coast, and is negotiating for a plant in Toronto, Canada, to be used as a manufacturing and shipping point.



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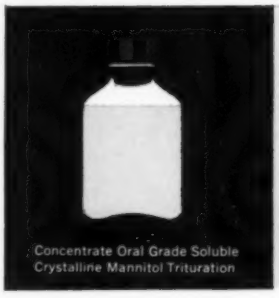

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Pfizer Vitamin B_{12} Crystalline 0.1% Triturations—for easier formulation of tablets and capsules, B_{12} is diluted to 0.1 percent with either mannitol or dicalcium phosphate. Each gram of this product equals 1 mg. of pure anhydrous B_{12}.

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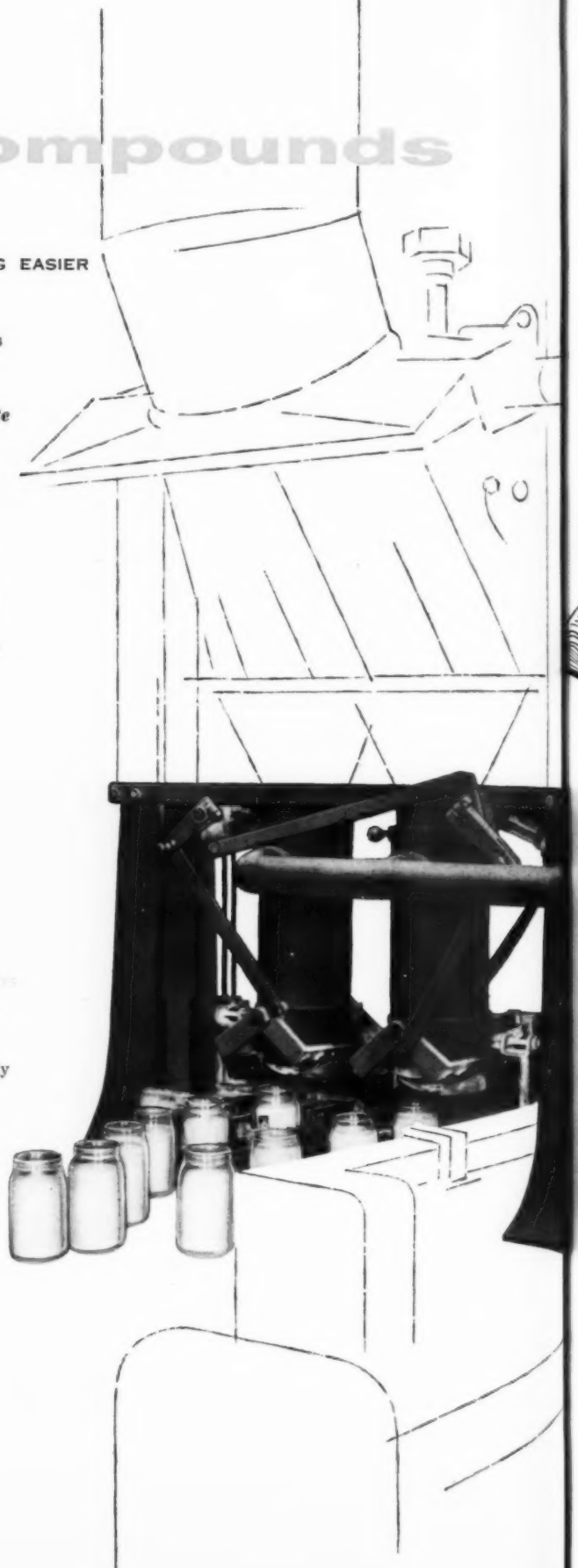

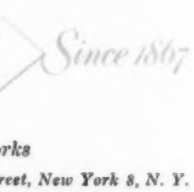

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Pharmaceutical PATENTS

The sharpness of competition in the pharmaceutical manufacturing industry has been apparent during the past several years. And as we have pointed out in the past, this competition reveals itself on several fronts. Because of the greatly increased number of companies in the pharmaceutical manufacturing industry, and because of the high stakes, many of the practices indulged in are not as ethical as those that this so-called ethical branch of the drug industry has been believed to employ. The sharp growth of the older leaders in the industry, the rapid rise of older, smaller companies to positions of prominence, and the firm establishment of many relatively newcomers to the field in the year since World War II has brought about these changes.

Competition in the pharmaceutical manufacturing industry is fought not only on the sales front and the advertising and promotional front, but it also fought in the research and development departments of the leading pharmaceutical firms. Sales methods in the industry have been more aggressive with greatly enlarged detail staffs as one of the weapons. Advertising expenditures have been upped in keeping with increased volume of sales. New products or different dosage forms or different variations of older products have been continually brought on the market in order to give the detail staff and the advertising departments something new with which to capture the attention of the medical and pharmaceutical professions.

But within recent years, many companies in the pharmaceutical field had risen to greatness, or had been baled out of a slump principally by products which were basically new. And in the case of several companies there had been only one product in each individual case. Furthermore, several of these products had been antibiotics. It is for this reason that numerous companies spent fortunes on soil-screening in the search for new antibiotics which might do what already discovered antibiotics will not do, or which might do the same things better and cheaper. But the enormous amounts spent on this search for antibiotics did not pay off in many instances, and some years ago Abbott Laboratories described the process in their financial report as "playing the slot-machine."

It turned out that good antibiotics are few and far between. It also turned out that a new antibiotic can be discovered by methods other than soil-screening. This was demonstrated by the discovery of tetracycline which was the result of research to determine the molecular structure of Terramycin and Aureomycin. If tetracycline should turn out to be the best broad-spectrum antibiotic discovered to date, as many predict, it would indicate that perhaps everything that can be discovered by soil-screening has already been discovered. Certainly one of the greatest difficulties of soil-screening is the rediscovery, over and over again at great cost, of antibiotics already in use. Then again, it seems that it is impossible to produce a product like tetracycline directly from soil or by fermentation without getting Aureomycin for the reason that there is always some chlorine present, and Aureomycin is chlortetracycline.

However, there seems to have developed in the pharmaceutical industry a desire on the part of many firms to add to their lines products of real promise regardless of the fact that someone else discovered them, and furthermore despite the fact that the one who discovered it might be entitled to patent rights. One such instance of recent years was procaine penicillin. Here is a product that was announced by a raw material firm and a pharmaceutical manufacturer. These two companies worked together on the development of the product. Immediately after the product was marketed by the company who was first, and who had applied for a patent, any number of other manufacturers of penicillin put out procaine penicillin. It was true that no patent had as yet been issued, and there was, or could not be any infringement until a patent was issued, but it did seem a rather strange procedure for the so-called ethical pharmaceutical manufacturers to follow. We asked one of them about it and where his company would stand if a patent were issued. His answer was that a patent might not be issued for a year or two, and things were moving so fast in the field that by that time there might be something better available which would obsolete procaine penicillin. However, the patent was eventually issued and several companies were licensed. However, others who were not licensed continued to

(*Continued on page 701*)

the CLEAR shampoo

CONDENSED FROM A FORTHCOMIMG BOOK

by Wm. R. Keithler

There are several variations of the clear shampoo, but for the sake of simplicity these shall be divided into two categories—soap and synthetic detergent-containing shampoos. The latter will be discussed first.

Of primary consideration in a clear shampoo are viscosity and cloud point. The viscosity of a shampoo can be controlled in any one of several ways, either by adding a gum, an organic thickener, or an inorganic salt, whereas the cloud point is slightly more difficult to control. The subject of cloud point will be discussed later in conjunction with the control of shampoos.

There is a long list of active materials that can be used in a clear, liquid, detergent-type shampoo. Best known are the triethanolamine, sodium, and ammonium lauryl sulfates. Their more important attribute is water solubility, and since the ammonium and triethanolamine salts display excellent water solubility, they are most often used. The pH, however, must be carefully controlled as a pH very far from neutrality may cause hydrolysis to occur.

The following formulation, using a sodium alcohol sulfate, has a cloud point of 44° F. and a viscosity of D to E, using the Gardner bubble method of viscosity determination. Ammonium chloride has been added as a thickening agent. Polyvinyl alcohol could be substituted.

No. 1

CLEAR LIQUID SHAMPOO

Sodium Lauryl Sulfate	46.0 per cent
Ammonium Chloride	5.0 per cent
Water	49.0 per cent

In a case where viscosity runs too high or too low minor adjustments can be made in the quantity of thickening agent used, or, in most cases, if the finished product is too viscous, simple addition of water will thin the product. The Gardner method of viscosity determination was used exclusively in all of these formulations, and an ideal consistency was placed at C to D.

No. 2

CLEAR LIQUID SHAMPOO

Triethanolamine Lauryl Sulfate	49.0 per cent
Polyethylene Glycol 400 Distearate	6.0 per cent
Water	44.0 per cent
Lanamine	1.0 per cent

The above formula has a viscosity of A to B and a cloud point of 38° F. Lanamine was incorporated to relieve somewhat the drying effects of the triethanolamine lauryl sulfate and to act as a hair conditioner. In the majority of shampoos the addition of lanolin will not be tolerated as it causes a definite clouding and also lowers the foaming properties. As a result of this, many lanolin derivatives have

been designed for use in shampoos as conditioning agents, and many are currently being used for this purpose.

No. 3
CLEAR LIQUID SHAMPOO

Triethanolamine Lauryl Sulfate	49.0 per cent
Polyethylene Glycol 400 Distearate	4.0 per cent
Water	47.0 per cent

The viscosity of the above formula is D to E and the cloud point is 70° F. The following two formulations have a relatively high cloud point of 69°. They are both shampoo concentrates which can be diluted for use in the approximate proportions of one pint of shampoo to one gallon of water to give a clear solution.

No. 4
CLEAR SHAMPOO CONCENTRATE

Sodium Lauryl Sulfate	50 per cent
Ammonium Chloride	1 per cent
Water	49 per cent

No. 5
CLEAR SHAMPOO CONCENTRATE

Sodium Lauryl Sulfate	30 per cent
Triethanolamine Lauryl Sulfate	20 per cent
Polyethylene Glycol 400 Distearate	5 per cent
Water	45 per cent

(*Continued on page 710*)

PHOTO COURTESY COTY INC

ZINC BACITRACIN in Pharmaceutical Preparations*

by Herbert M. Gross, Ph.D.

HEAD, DEPARTMENT PHARMACEUTICAL DEVELOPMENT, PHARMACEUTICAL RESEARCH DIVISION, COMMERCIAL SOLVENTS CORPORATION, TERRE HAUTE, INDIANA.

Because of the safety, versatility, low order of antigenicity and therapeutic effectiveness in topical and oral application, bacitracin is being used in many pharmaceutical preparations. The antibiotic has been widely investigated and recognized as an effective chemotherapeutic of considerable application. Bacitracin, chemically thought to be a polypeptide, is produced by the Tracy strain of *Bacillus subtilis*. It is potent against a wide variety of gram-positive organisms; Hemolytic and non-hemolytic streptococci, Staphylococci, Anaerobic cocci, Pneumococci, Clostridia of the gas gangrene group; Corynebacteria; certain Gram-negative cocci as: gonococci, menigococci; Spirochetes of syphilis, pyorrhea, Vincent's infection; Actinomyces; *Endamoeba histolytica*; and *E. vermicualris*.

Many applications and formulations of bacitracin have presented problems relative to antibiotic stability, heat lability, compatibility and taste. In the same manner in which the procaine salt of penicillin solved many penicillin problems, zinc bacitracin has resolved many of the problems concerned with formulation and stability of topical and oral pharmaceutical products containing bacitracin.

The Federal Register, section 146a.418 defines "zinc bacitracin as the zinc salt of a kind of bacitracin or a mixture of two or more such salts. It is so purified and dried that:

1. Its potency is not less than 40 u/mg.
2. It is non-toxic.
3. Its moisture content is not more than five per cent.
4. Its pH is not less than 6.0 or more than 7.5.
5. Its zinc content is not more than 10 per cent by weight on a moisture free basis."

The Federal Register allows a 24-month outdate on the bulk, certified raw material, zinc bacitracin. Recently, the Food and Drug Administration recognized zinc bacitracin in troche preparations in all the antibiotic combinations heretofore accepted with bacitracin.

*Presented, in part, at the meeting of the Research and Development Section, American Drug Manufacturers Association, Atlantic City, New Jersey, October 7-9, 1954.

Chemical and Physical Properties

The certified bulk zinc bacitracin as commercially available in addition to meeting the requirements set forth by the Food and Drug Administration, is produced with the following inner specifications:

1. The potency is usually between 50 u/mg and 60 u/mg of bacitracin activity.
2. The moisture content may vary between one and four per cent.
3. The pH may vary between 6.0 and 7.0.
4. The zinc content, on a moisture-free basis may vary between 4.3 and 7.0 per cent.
5. The material will pass 99.5 per cent through a 100 mesh, U. S. Standard sieve, but may be available in various particle size fractions if necessary for specific formulation.
6. The bulk density of the zinc bacitracin is suited to both tablet and ointment manufacture.
7. The product must meet the heat stability requirement that it shall not lose more than 15 per cent of its activity in eight hours at 105° C.
8. The product meets the solubility requirement that not more than 0.5 per cent by weight is soluble in water at 25° C.

These additional qualities are valuable to the formulator and the pharmaceutical manufacturer for the development and processing of a product with stability and pharmaceutical elegance.

It is of advantage to use an antibiotic of higher potency per unit weight in that it enables the manufacture of tablets of lesser weight and size, allows the preparation of ointments with a lesser bulk of solids to disperse in the base and reduces by up to 40 per cent the shipping weight of antibiotic. Since it has been accepted that the presence of moisture is deterrent to the activity of bacitracin and its salts, a lesser moisture content is obviously of value in the stability of the antibiotic. Closer values of tolerance in pH indicate a more controlled process resulting in a uniform product. The control of the zinc content is likewise reflected in product uniformity. The availability of a product of the desired

particle size and bulk density is of value in eliminating costly pre-working of raw materials prior to the production of pharmaceuticals.

The relative stability of zinc bacitracin as compared to bacitracin is reflected in its heat stability requirement. This quality enables the antibiotic to be formulated in heated ointment bases, in oven-dried tablet granules, in troches prepared by the hard-candy fusion method and in a variety of pharmaceutical dosage forms requiring high temperature unit operations. A study carried out at 105° C. on bacitracin and zinc bacitracin indicated the thermal stabilities of the antibiotic and its zinc salt.

THERMAL STABILITY OF BACITRACIN AND ZINC BACITRACIN POWDERS AT 105° C.

Time (Hours)	Per Cent Loss in Activity	
	Bacitracin	Zinc Bacitracin
½	3.0	0.4
1	6.2	0.0
2	11.5	2.5
4	18.8	3.5
8	30.0	8.6
24	46.2	17.5

Additional data of interest indicative of thermal stability of zinc bacitracin was collected from an in progress stability study of a 50 unit per milligram lot stored at various temperatures in sealed containers.

THERMAL STABILITY OF ZINC BACITRACIN POWDER AT VARIOUS TEMPERATURES

Time (Months)	Per Cent Retained Activity		
	Stored at 25° C.	40° C.	60° C.
6	100	100	100
9	100	100	100
12	100	100	97
18	100	100	94

The tastelessness of zinc bacitracin is inherent in its relative insolubility. Solubility determinations of production lots of zinc bacitracin indicate a water solubility at 25° C. of 0.23 to 0.45 per cent by weight. The ability to produce a salt of low solubility is indicative of product purity and points to use of the zinc salt in preparations where taste is a factor. A U. S. patent application has been filed on an antibiotic-containing troche, a therapeutic preparation containing zinc bacitracin, on the basis of the relative tastelessness of the product obtainable by the use of zinc bacitracin rather than bacitracin.

Toxicology

Consideration of the toxicity of the antibiotic is elementary and is reflected in the uses to which it is applied. Various toxicities were determined on this salt, and accumulated data indicated its safety in topical and oral administration. The acute oral toxicity studies in mice indicated that the LD_0 varies between 2000 and 5000 mg./Kg. A study of a 58 unit per milligram lot indicated the following acute toxicities in mice: LD_0 3000 mg./Kg., LD_{50} 4480 mg./Kg. and LD_{100} 5000 mg./Kg. Subacute toxicities were carried out on mice by administration of dosage levels of 2240, 1120, and 560 mg. of zinc bacitracin per kilogram weight per day for 14 days. Mice receiving 1120 mg./Kg./day gave the same toxicity results as those control mice receiving the equivalent of normal saline administered orally. In dogs, no toxic effects were noted with single oral doses of 10,000 units of zinc bacitracin. Chronic toxicity studies in dogs in which 4000 units per day were administered orally for 30 days indicated no detectable change in blood count, hemoglobin or NPN. No gross pathology was noted, but a slight irritation was exhibited in some intestinal mucosae. This was attributed to a probable astringent action of the zinc ion.

A study was made of the toxicity of zinc bacitracin as compared to bacitracin. In comparable oral doses, no difference was indicated between the effects of bacitracin and zinc bacitracin on tissues of dogs, rats and mice. Rats administered bacitracin orally 1000 mg./Kg./day and rats fed zinc bacitracin 1000 mg./Kg./day showed no significant physiological difference or microscopic lesions.

The possible irritating effect on the skin by zinc bacitracin in ointments was investigated. Ointments containing 500 units per gram of zinc bacitracin were

(*Continued on page 684*)

Modern Treatment

Acne vulgaris is one of the most common of skin diseases—one that often has a marked effect on the person suffering from it. Coming, as it usually does, during adolescence, when so many adjustments to life must be made, it is important that this condition be given proper treatment if cosmetic and psychic scars are to be avoided. Physicians now realize that active and effective therapy is essential for what, in former years, was often looked upon as a trivial matter. This modern attitude is reflected both in the keen interest in the causes of acne and the constant trial of new preparations for its improved treatment.

As remarked by Sulzberger,[1] acne is still one of the greatest dermatologic problems, and its management is still the major activity of most dermatologic practices. Statistically speaking, it has been estimated that more than half the population is subject to acne and some authorities go so far as to say that no one escapes the disease, at least in a mild form.[2] Kile,[3] for example, says that it is rare for anyone to go through adolescence without a few acne comedones. He points out, however, that while acne is primarily a disease of adolescence, it is by no means limited to that age group. The condition is seen during the menopause as well as premenstrually in many otherwise normal women. It is not uncommon, says he, to see new patients with acne in their late twenties and early thirties.

Acne vulgaris is described[4] as an inflammatory process of the skin involving the sebaceous follicles. The eruption usually consists of plugged follicles, with blackheads (comedones) or whiteheads in the openings; perifollicular inflammation and induration, forming reddish, elevated papules, and pustates. In addition there may be seborrheic scaling, with or without oiliness of the scalp, oiliness and thickening of the skin, and enlargement of the sebaceous glands and their openings.[5] The face, particularly the middle third, the chest, and the upper back are commonly involved.

Neglect of the condition may result in marked disfigurement and permanent scarring. It is stressed[6] that when acne is severe, persists beyond the 'teens, or recurs in adult life, it may seriously interfere with social activities and make work impossible in humid climates, hot surroundings, or with oil contacts. Attention must then be directed to the factors contributing to these manifestations, including diet, drugs, hormonal and psychic influences, greasy contacts, lack of soap, and climatic conditions.

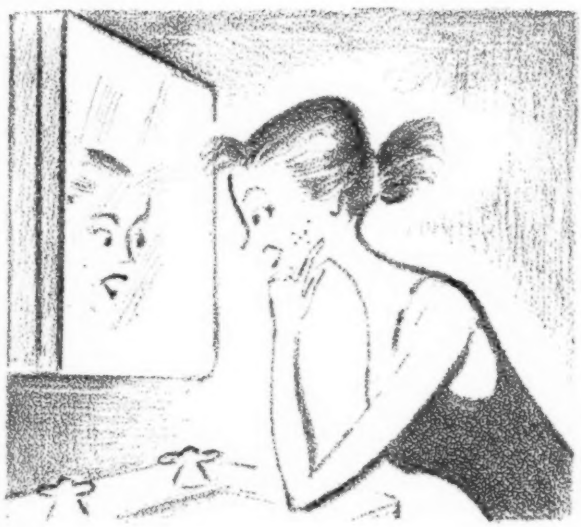
These are but a few of the many factors which influence acne. Some workers feel that hormonal imbalance and psychic factors are of primary importance in the causal picture.[6,7] Lorenz and his associates[8] have shown that in patients with acne, emotional stress is associated with increased sebum secretion. On the basis of their broad clinical experience, Andrews and his colleagues[9] are of the opinion that emotional factors are extremely important in acne. They point to the close relationship of acne to puberty and the sex hormones and to the effects of these forces upon the emotions. There is no doubt, say these dermatologists, that as the skin condition subsides from the use of hormones and other remedies, the patient becomes happier, more contented and less detached from society.

However, many considerations enter into the treatment of acne. Obviously, treatment must be individualized, and there are various effective measures available to help clear up the lesions and produce a cure in many cases. Much depends on the extent, number and depth of the lesions, the degree of pydermic involvement, constitutional make up, and the emotional impact of the acne on the patient. Basically, treatment should aim at lessening the activity of the sebaceous apparatus, eliminating secondary infection, and cosmetic improvement. Where indicated, such factors as constipation, hypothyroid activity and anemia should be corrected, and dandruff should be eradicated.[10]

Although, as noted by Kline,[11] there is no agreement as to the mechanism by which certain foods produce or aggravate acne, diet is still recognized as an important factor in influencing the course of the disease. According to Andrews and his associates,[9] the chief features of a suitable diet are the avoidance of excessive amounts of fatty and fried foods and sweets and the eating of plenty of fruit, cereal, meat and vegetables. Chocolate, nuts, ice cream, cream, egg yolk, and cheese should be avoided, and milk should be limited to a glass or two per day.

It is generally recognized that foods rich in iodine, such as shellfish and sea food, must often be eliminated from the diet. Iodized salt has been found to aggravate

# of ACNE *by Milton A. Lesser*



acne and should be avoided by those with this disease. Such people should also be cautioned not to take medicines containing bromides or iodides.[3,12]

Adequate vitamin intake is, of course, an integral part of the dietary regimen. However, large vitamin A supplements appear to be useful in many cases of acne. It has been found that the oral administration of vitamin A is of benefit in cases of acne in which comedones and follicular horny plugs dominate the picture.[12] In the presence of many comedones, the vitamin A dose ranges from 100,000 to 200,000 units per day, and this dose must be continued for three to six months before its effectiveness can be determined.[9]

The effectiveness of large doses of vitamin A in the treatment of acne vulgaris has been indicated in the report of Lahiri and Scandrett[13] on a series of 75 patients who had resisted other forms of therapy. With oral vitamin A, in a daily dose of 100,000 units as the sole treatment, it was found that the time taken for the disappearance of lesions was two and one-half months in 30 cases, three months in 30 cases, five and one-half months in 10 patients, and six months in the remaining five. Although some patients required longer treatment, all could be regarded as cured at the end of six months.

Some physicians[11-14] prefer to prescribe the newer aqueous forms of vitamin A because better absorption and lower dosages are possible. According to Day and Anderson,[15] therapeutic blood levels are attained with 25,000 to 50,000 units daily, but prolonged administration may be needed to obtain improvement. In tests with an aqueous dispersion of synthetic vitamin A, Becker[16] obtained improvement in 41 per cent of 106 patients, of which nine were entirely cured. All but one of the patients benefited by vitamin A had acne of the papular-comedone type.

Aqueous dispersions of vitamin A are sometimes administered parenterally in severe cases of comedones.[9] When the oral use of vitamin A is ineffective, Kline[11] has found that responses can often be elicited by intramuscular administration of the vitamin. Frequently, says he, a combination of oral aqueous vitamin A with parenteral vitamins (Vi-Syneral Injectable) achieves a maximum response.

Local measures play an important part in the treatment of acne. As noted by Sulzerber and Wolf,[5] the general objective of local treatment is to produce a scarcely perceptible peeling, just sufficient to open the papules and pustules and to remove the comedones. Medication must be adjusted with this end in view and the skin should be kept on the "dry side" during the acne age.

Proper cleansing of the skin is a major element in the local treatment of acne. If used regularly with a washcloth or complexion brush, soap and water are valuable measures in dissolving and removing follicular plugs. The number of washings per day will depend on the degree of oiliness of the skin and its tolerance for repeated washing.[12] Oiliness will also be a determining factor in selecting the most suitable soap. For darker or oilier skins a mildly abrasive soap may be used (e.g. Lava) while for fairer complexions, a conventional milled toilet soap is more satisfactory.[2] In addition, synthetic detergents, which have a drying effect, are available and many patients with oily skin do well with such preparations.[3]

As mentioned by Lubowe,[17] soaps containing hexachlorophene are being used for their bacteriostatic effect. Day and Anderson[15] similarly note that antiseptic soaps, notably those with hexachlorophene, if

used frequently, help to prevent self inoculation that occurs from spreading the purulent material in the severely suppurative forms of acne.

Lotions play a prominent part in the local treatment of acne vulgaris. Such preparations, which generally contain sulfur or resorcinol (resorcin), or both, as the active agents, are used primarily to induce peeling and depress the sebaceous system. The selection of the most suitable lotion depends upon such considerations as therapeutic efficacy, frequency of application required, appearance on the skin, degree of skin oiliness, mechanics of application, and ease of removal.[15]

Sulfur in some form is the basis of most acne lotions; its effects being a depression of the sebaceous secretion and a mild antiseptic action. In England, Wrong[18] obtained "excellent" results in 75 per cent of cases of acne treated with Mackie's special sulfur lotion. This consists of:

Sulfur	7.5 parts
Sodium mixed alloyl benzene sulfonate	110.0 "
Antipyrene	54.0 "
Triethanolamine	100.0 "
Propylene glycol	560.0 "
Water	168.5 "

For sensitive skins, where even a small amount of sulfur may be irritating, Swartz[4] recommends the following lotion:

Zinc oxide	8.0 Gm.
Calamine	4.0 Gm.
Phenol	2.0 Gm.
Glycerine	8.0 cc.
Spirits of camphor	8.0 cc.
Water, distilled, to make	240.0 cc.

There is a growing awareness that acne lotions can be both therapeutically effective and cosmetically acceptable. Realizing that patients with acne will not use medicaments that are conspicuous on the skin during the hours of social contact, doctors now prescribe or recommend preparations that are suitably tinted to match the complexion. Illustrative of this trend is a shake lotion in which the amounts of calamine and neocalamine are varied to meet the needs of the individual case. As prescribed by Messina,[14] the lotion contains:

Sulfur, precipitated	6.0-12.0 parts
Resorcin	2.0 "
Boric acid	4.0 "
Glycerine	4.0 "
Calamine	5.0-15.0 "
Neocalamine	5.0-15.0 "
Witch hazel water	60.0 "
Water, to make	180.0 "

This is applied twice daily, but applications are reduced or stopped for a short time if excessive dryness occurs.

Acne lotions in various skin tints are now being marketed to permit continuous therapy, including the daytime hours. Some of these preparations contain varying amounts of pigments in order to help hide the lesions.[3] Flesh-tinted creams for treating acne are also available from a number of pharmaceutical houses.

Ointments are sometimes used in the topical treatment of acne, but there are those[15] who feel that preparations of an oily or greasy nature have little place in the therapy of this condition. However, the so-called washable or greaseless creams containing sulfur, resorcinol or both are quite popular and are often useful for patients who complain of the drying effects of lotions.

Indicative of the modern trend is the following pigmented preparation which, in addition to being more cosmetically acceptable, serves to cover and conceal minor lesions of the face:

Sulfur, precipitated	2.0 Gm.
Resorcinol	0.5 Gm.
Titanium dioxide	4.0 Gm.
Pigment	sufficient
Emulsion base, to make	100.0 Gm.

The emulsion base required in this preparation consists of:

Polyethylene glycol 200 monostearate	15.0 Gm.
Magnesium aluminum silicate	2.5 Gm.
Polysorbate 80	1.0 Gm.
Methyl *para*-hydroxybenzoate	0.1 Gm.
Water, distilled, to make	100.0 Gm.

In presenting the above formula Frazier and Blank[19] stress that the tinting of this preparation with titanium dioxide and pigments accepted by the Food and Drug Administration adds foreign material to the cutaneuos surface. This can block the openings of the follicles unless it is subsequently removed by thorough washing.

As previously mentioned, several skin-tinted creams for treating acne are now on the market. One such (Acnomel), containing two per cent resorcinol, eight per cent sulfur and 11 per cent alcohol in a flesh-tinted nongreasy base, was tested by Dexter.[2] Patients using this local medicament showed more rapid response than those treated with other preparations. The cream decreased the sebaceous secretion and was adequately keratolytic and antiseptic for all except deep pustules. The cosmetic effect of the cream made it possible to mention active treatment during the day as well as at night. The tinting, which matched the average skin, permitted the patient to cover the lesions, thereby preventing embarrassment and lessening the tendency for self-traumatization during treatment. In passing, it may be mentioned that the suppliers of this cream have also marketed a cosmetic-type cake containing four per cent sulfur, one per cent resorcinol and 0.25 per cent hexachlorophene in a washable, flesh-tinted cake base.

Recently, Kline[11] reported excellent results from the use of a preparation (RS Panthoderm Cream) incorporating sulfur and resorcinol monoacetate in a water-miscible base containing pantothenylol, which acts as a

(*Continued on page 717*)

mascara and EYE make up

by Harry Hilfer

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Eye make ups are perhaps the oldest types of cosmetics, since women, from the earliest civilizations onwards, have attempted to accentuate the beauty of their eyes. In their present forms, mascaras and eye shadows still have the same function. The differences between the past and present forms lie in the relative ease of application of the modern products. In the formulation of products for use in the area of the eyes there is a broad limitation imposed by law—the limitation of the choice of colorants to natural dyes and inorganic and carbon pigments. In common practice, therefore, the commercially available pigments used are the varying shades of the iron oxide pigments, the different carbon blacks and ultramarine blues. These colorants, though adequate for use as mascara and eye shadows, leave little room for the creation of some of the sought-after special effects, and as a result there has been no attempt to introduce new color fashions in these products, as is possible, for example, with lipsticks.

The accentuation of the eyes is best achieved by emphasizing the eyelashes, which is the function of the mascara. The addition of the color to the lashes not only makes them appear more highly colored, but also longer, since in many instances the ends of the lashes tend to be rather blondish as compared to the rest of the hair length. The film applied should show good resistance to moisture since the eyes may tear and cause smudging, as well as be resistant to gentle abrasion, as would happen if the hand should be brushed across the eyes. The best-known form of the mascara is perhaps the so-called cake mascara which is used in conjunction with a wet brush. The most modern forms depend on the use of an oil-soluble soap which, on gentle brushing with water, forms an emulsion containing the colorants and the rest of the mascara vehicle. After application of the emulsion to the lashes the film is allowed to dry and in this way the lashes may be colored, and the colors protected by the rest of the dehydrated vehicle. In such a system, the greater the amount of soap used, the easier would be the formation of an emulsion with water. This tendency must be balanced against a water-resistant agency also needed in the system to protect the film against accidental contact with water. Carnauba wax is usually used to impart this factor. The final preparation should therefore be a compromise between water repellency, as represented by the waxes, and other hydrophobic substances used, but which cannot be applied readily without the presence of a compatible hydrophilic substance, as represented by the oil-soluble soap. The ideal combination would be a minimum soap concentration, with enough to form an emulsion, and a maximum amount of waxes, but not so much that emulsion formation would be impeded.

This sort of a balance would seem to indicate that the film would be prone to easy attack from water, but it is possible to formulate the product so that the water repellency feature becomes predominant. Since the emulsion is formed with the aid of relatively vigorous trituration with a stiff bristled brush, it would not be easily reformed by casual contact with water after dehydration of the film. Advantage must therefore be taken of the use of the brush in application as a mechanical means necessary for emulsion formation, which means is no longer present after application and dehydration.

A triethanolamine soap is the most commonly used hydrophile, since these soaps are rather readily soluble in waxes or other esters. Carnauba wax is perhaps the major wax constituent of the formula and its choice is dictated by its high melting point and its inclination towards producing a highly water-repellent film. A good range of colors may be made from members of the classifications already referred to. Many formulators have found that Carnauba wax has too high a melting point to be conveniently used to the exclusion of other hydrophobic agents, and they therefore include waxes of lower melting points so that actual production

(*Continued on page 703*)

*Animal Skin for Testing Chemicals**

by L. W. Hazleton, Ph.D.
HAZLETON LABORATORIES, FALLS CHURCH, VIRGINIA

What is the objective to be achieved by evaluating chemical reactions on animal skin? In the day-by-day operation of the laboratory our technical staff is faced with the problem of designing experiments to provide the answer to many questions based on skin reactions.

Our only real objective in evaluating skin reactions following application of chemicals is to achieve answers to specific questions. The vast volume of work conducted along these lines is that of evaluating hazards which might result from dermal exposure to chemicals. In our rapidly expanding chemical economy new chemicals are the rule rather than the exception. We have long ago learned that each chemical poses a hazard until evidence indicates otherwise.

This hazard, which may be defined as the probability of injury following exposure under conditions of use, may take the form of irritation, contact dermatitis, sensitization, or outright and frank systemic toxicity.

A second question to be answered is whether or not a chemical might have a therapeutic effect. By definition a therapeutic effect would have to be achieved following application to diseased or otherwise damaged skin. A third important question is whether or not a chemical might have some beneficial effect on normal skin. The use of the term, "normal," in this connection poses many questions which are all too familiar to this group. Equally the question of diseased, pathological, or traumatized skin poses many problems of definition.

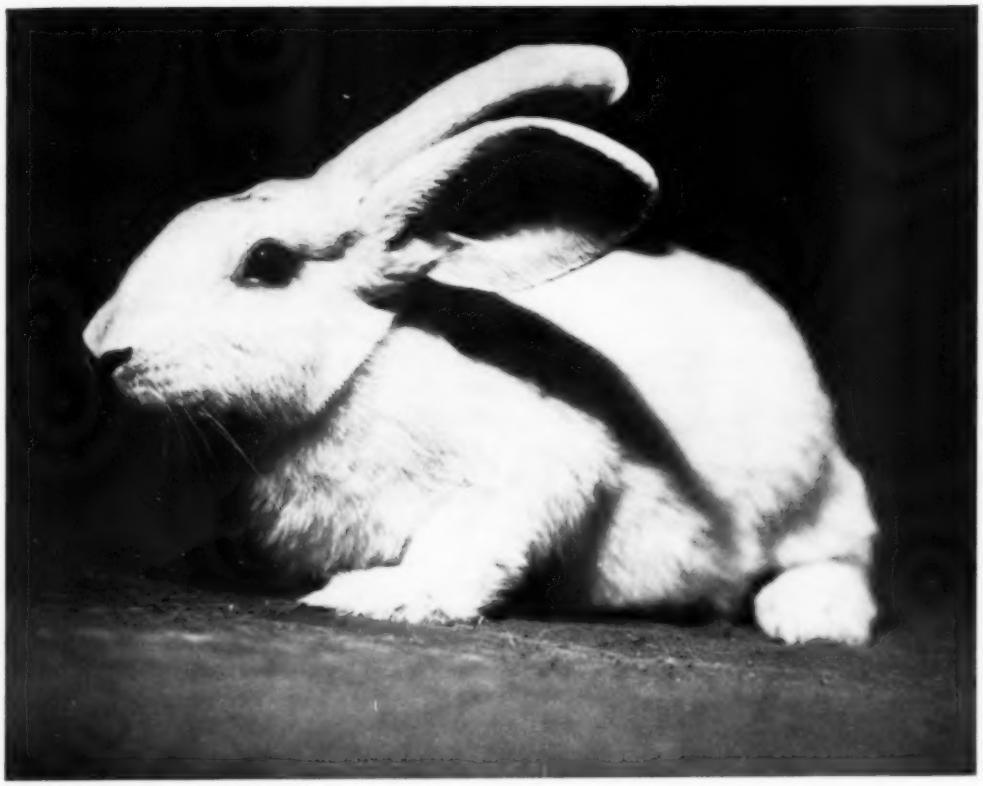
Hazard evaluation can be a fascinating study, and extremely complex experimental designs have been proposed. These are aimed at placing the proper emphasis on a large number of variable factors, including concentration, total duration of exposure, total surface of exposure, physical state of chemical subdivision, effect of repeated discrete exposures, and the simulation of conditions approximating the probable exposure under conditions of use. In the broadest sense the two general reactions observed in this type of study are systemic toxicity which follows absorption of the chemical through the skin and into the blood stream, or those of local, strictly dermal reactions. From the cosmetic standpoint each and all of these studies can be of interest. It is well to know, for example, that under severe conditions of surface concentration and exposure time a given chemical appears to cause no local or systemic reaction in animals. While this knowledge is the answer to the original question of hazard, it might also have a secondary interest to the cosmetic chemist were he aware of such data. Certainly here would be a chemical which could be of cosmetic interest and on which a preliminary assumption of safety for use could be made.

The alternate result from the above example may be that the new chemical was irritating at various concentrations but under certain conditions was not injurious to the skin. This would be the answer to the question of industrial or chemical hazard, but it is far from the answer to whether or not there might be a cosmetic interest. As I have pointed out on other occasions, and as others before me have pointed out, there is a vast amount of investigation required to bring our knowledge of cosmetic chemical potential up to anywhere near a current status.

To move on quickly to the second objective, that of therapeutics, we again face the problem of whether or not a material which is therapeutically beneficial to diseased or traumatized skin might be also cosmetically beneficial under proper conditions and for clearly defined objectives. The cosmetic industry uses many such materials; for example, lanolin, mineral oil, vitamin-containing creams, benzoin, and analogous materials. One may well question, however, whether the cosmetic industry is keeping pace with the development of new materials for therapeutics and their proper evaluation in cosmetic terms. It is to be hoped that the industry is abreast of this development so that it may take advantage in the future of what it has learned in the past.

The question of investigating for other beneficial effects perhaps poses the greatest problem of all. Various types of skin, skin coloring, blemishes, age, texture, and exposure are all important aspects in evaluating beneficial effects. Here, unfortunately, our experience lets us down somewhat. The cosmetic effect is best evaluated by sensory perception; namely, visual, olfactory, and tactile. As a continuous pro-

*From a paper delivered at Society of Cosmetic Chemists Seminar September 23.



EWING GALLOWAY PHOTO

cession of seminars attest, the standardization and comparison by sensory perception is an extremely unreliable field. We are faced, therefore, with the problem of methodology to assist in the standardization of sensory responses. Certainly this would require an additional seminar by experts in many fields for one even to begin to appreciate the depths of this problem.

From the above it is apparent that the cosmetic industry does have an interest in practically all skin evaluation whether they are fully aware of this or not. If cosmetic chemists are interested in a particular chemical or variation of formula, whether this has been brought to our attention through the magnanimous efforts of the sales representative or through deductive reasoning on their own part, it is my belief that animal skin evaluation fulfills many steps of the procedure in a manner superior to human testing. While animal skin and human skin have major and important differences, experience has shown us certain major fields in which animal skin may be used to predict human skin reaction. Animals have the additional advantage of being readily available, quite controllable, and devoid of the individual rights and prerogatives which we like to associate with our fellow man. Their standardized living, standardized breeding, and relative space requirements are certainly advantages from a scientific experimental design and cost standpoint.

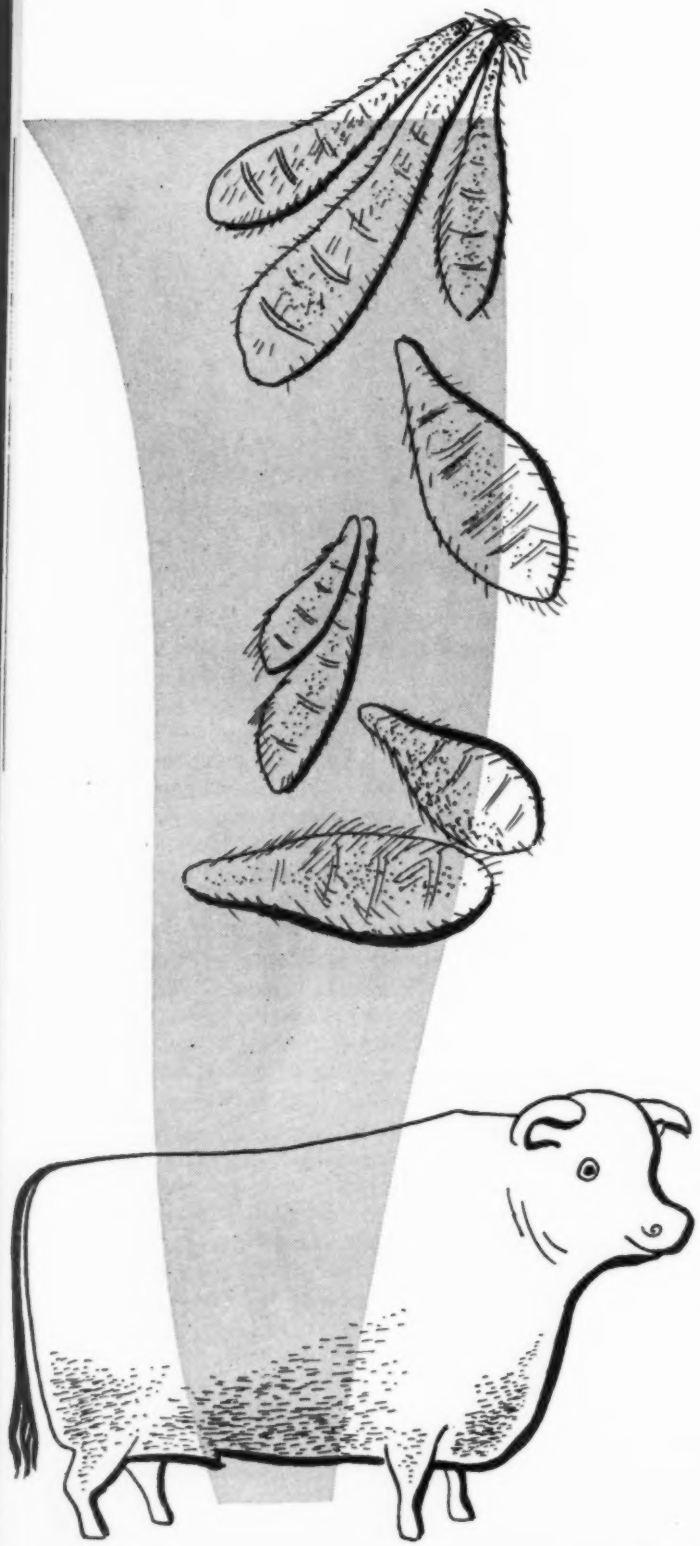
Of the three major cosmetic interests—irritation, sensitization, and aesthetics—it would appear that the experimental animal serves his greatest function in the field of irritation. We in our laboratory feel that the use of animals is an essential preliminary in the evaluation of any new chemical, and that the future of cosmetic chemistry lies in the exploration of vast numbers of new chemicals rather than the miscellaneous juggling of old chemicals into new and slightly different formulations. Our staff physicians are extremely reluctant to expose any panel of human subjects to new chemicals until after the animal tests are completed. Choice of animals is of importance but mostly is related to personal experience of the investigators. Rabbit skin can, I think, be said to be somewhat more sensitive to chemical irritation than the average human skin. Guinea pig and rat skin are widely used for irritation studies, however, and so long as the investigator has the background of comparative evaluation between the animal and human, it makes really very little difference which animal is selected. It is quite possible that the use of swine will become much more popular than it has been in the past if some of the miniature breed programs now under way turn out successfully.

Pharmacologically, irritation is synonymous with stimulation, and one should not overlook the fact that a very mild degree of irritation which is controllable and reproducible may be exactly what one is seeking for certain cosmetic applications. Certainly it is the basis for much therapeutic pharmacology.

As mentioned earlier, methodology is the big problem in evaluating irritation critically. Severe irritation, including necrosis, is of course readily observable but not readily comparable from one chemical to another.

(Continued on page 714)

Steroid HORMONES



Quite recently a number of investigators in England and in this country have isolated a powerful sodium-retaining substance in adrenal vein blood of various mammalian species which is probably the newly isolated adrenal steroid, aldosterone. Thus it seems that the chief, and perhaps the only, steroids normally released by the adrenal cortex are hydrocortisone, corticosterone and presumably aldosterone.

Desoxycorticosterone has been of great value to the experimentalist working with adrenalectomized animals and to the clinician for use as substitution therapy in controlling Addison's disease. Until recently it ranked first in potency among adrenal hormones for its effect upon mineral metabolism and maintenance of normal health and vigor of adrenalectomized animals and Addisonian patients. It exerts profound renal effects upon sodium retention, potassium excretion and internal distribution of water and certain electrolytes. In fact, the potency of this hormone is so great that serious overdosage effects may occur in man and animal. In improperly controlled doses especially when the salt intake is not restricted, the compound may cause hypertension, oedema, increased blood volume, substitution of sodium for potassium in skeletal and heart muscle cells and other disabilities. In the early days of desoxycorticosterone therapy, before the limitations of the steroid were realized, the Addisonian patient was sometimes in as much danger from the treatment as from the disease. However, due to the labors of clinicians, physiologists and research pharmacists the steroid has now taken its rightful place along with other hormones in the armamentarium of the physician.

Although desoxycorticosterone was a boon to patient and physician, it was soon realized that it does not completely substitute for the adrenal cortical secretions. It lacks an important function, viz., ability to maintain adequate carbohydrate reserves in fasted adrenalectomized animals and Addisonian patients. It is also unable to sustain such animals or patients when they are subject to stress. Since the compound is practically insoluble in water and must be used in oily solutions, it is limited in its effectiveness during periods of adrenal crisis. Such individuals are desperately ill and hence radical remedial measures are necessary involving intravenous salt, glucose, fluid and cortical extract in large quantities. To meet this shortcoming of the steroid, the pharmaceutical staff of the Ciba Company in Basle undertook to solubilize the compound in an

*From a paper delivered before Columbia University College of Pharmacy Bicentennial Conference, October 14, 1954.

in Medicine*

by W. W. Swingle BIOLOGICAL LABORATORY, PRINCETON UNIVERSITY.

aqueous medium for use intravenously. Their efforts succeeded and now it is possible to obtain the water soluble glucoside of desoxycorticosterone. The material is non-toxic in so far as my coworkers and I have been able to determine in large scale experiments on normal and adrenalectomized dogs. It is highly effective by vein, in our experience, the most effective way to revive animals lacking adrenals from severe insufficiency. It exhibits only mild overdosage effects even when administered in enormous doses since there is no cumulative effect due to slow absorption of an oil solution. European physicians have reported using the material successfully in Addison's disease but to my knowledge it has not been widely tested on patients in this country.

The demonstration by Hench, Kendall, Slocumb and Polley of the efficacy of intramuscular injections of fine crystalline suspensions of cortisone in rheumatoid arthritis aroused interest in testing suspensions of other adrenal steroids. The Ciba Pharmaceutical Company prepared the trimethylacetate and phenylacetate of desoxycorticosterone and it was shown by Meier that the trimethylacetate preparation when given in oil as a single intramuscular injection of 10 mg would maintain the adrenalectomized dog in good health for 35-40 days. Thorn made a clinical test and reported that 60-120 mg, when injected intramuscularly into an Addisonian, controlled sodium metabolism for two months. These observations stimulated workers in my laboratory to study both the trimethylacetate and phenylacetate of desoxycorticosterone in adrenalectomized dogs. Briefly stated our experiments showed that a single injection of a crystalline suspension of 10 mg. of the trimethylacetate was sufficient to keep the animals active, healthy and entirely free from symptoms of adrenal insufficiency for periods ranging from 50-60 days. Similar injections of the phenylacetate maintained the dogs symptom free for 40-46 days. The animals remained lively, ate full rations and maintained their weight until a few days before termination of the test. Various other crystalline suspensions of desoxycorticosterone and other steroids were tested but none gave results on life maintenance at all comparable to the trimethyl and phenyl acetates. Gaunt, Leathen and associates have performed similar experiments using adrenalectomized rats. To my knowledge none of these desoxycorticosterone preparations is effective in diseases other than those due to failure of the adrenal glands such as occurs in Addison's disease.

A new and significant addition to knowledge of the chemistry and physiology of the cortex during the past year, has been the isolation and determination of the structure of aldosterone. It has long been recognized that after removal of all of the known crystalline compounds from cortical extract concentrates, there still remained in the mother liquor an active, non-crystalline residue designated simply as the amorphous fraction. Interest in determining the nature of this material was revived and greatly stimulated by the experiments of Tait, Simpson and Grundy published in a series of papers between 1952-1953. These investigators devised a simple and rapid method for determining in a quantitative manner, the sodium-retaining activity of adrenal steroids on adrenalectomized rats. Using their method of assay they demonstrated the presence of a powerful sodium-retaining substance in adrenal vein blood; similar material was also found in extracts of beef glands which upon assay proved to be twenty-five times more potent than desoxycorticosterone acetate, which up until this time was regarded as the most powerful sodium-retaining steroid. Recently other workers in this country have obtained evidence for the presence of a similar substance in the urine of children with nephrosis and in blood from the adrenal vein of dogs. These studies clearly indicated the existence of an unknown hormone presumably steroidal in nature which possessed surprising mineralocorticoid activity.

Simpson and Tait, in collaboration with the Swiss chemists Reichstein and his group and Wettstein and his coworkers, soon isolated a pure crystalline compound from adrenal extracts which upon assay exerted an effect on sodium retention far greater than that displayed by desoxycorticosterone acetate. The compound was provisionally designated as electrocortin and in the first reports was said to be 30-100 times more active than DCA depending upon the test and animal employed. Two groups of investigators in this country announced the results of their studies on the sodium-retaining factor only a few weeks following the publication of the paper by the British and Swiss workers. Mattox, Mason and their associates at the Mayo Clinic, obtained crystals which posessed mineralocorticoid activity equal to twenty-five times that shown by DCA. Knauff, Nielson and Hains, working at The Upjohn Company obtained non-crystalline but extremely potent sodium-retaining material.

The chemical constitution of the new steroid was established by the Simpson, Tait, Reichstein group, and aldosterone was suggested as a definitive name for the compound. There is general agreement that it is far

(Continued on page 707)

The Role of Drugs

Many of us tend to regard a drug as a medicinal substance not normally involved in the life processes. Such a concept would of course exclude the nutrients—the vitamins, minerals, carbohydrates, and components of protein and fat. Moreover, the study of their effects is generally considered the province of physiology rather than pharmacology. Such distinctions are useful, but somewhat arbitrary, for difficulties arise if we attempt to distinguish nutrients from drugs on the basis of function. The borderline grows hazy as studies reveal increasingly that substances intrinsic to metabolism, when applied under certain conditions, may have a medicinal function bearing no apparent relation to their usual metabolic role. I will try to illustrate that under certain circumstances *nutrients are drugs*, in the sense that they can correct abnormalities caused by factors other than diet.

One such abnormality is the neuritis produced by isoniazid, the now-famous agent recently found useful in tuberculosis. This compound is structurally related to niacin and pyridoxine. It is doubtful that niacin antagonism plays a part in the toxicity, since clear-cut signs of niacin deficiency are absent. On the other hand, a close resemblance between the neuritis and that induced by desoxypyridoxine, a vitamin-B_6 antagonist, led Biehl and Vilter to investigate the effects of B_6 administration. Of 36 control patients that received only isoniazid, 14 developed neuritis; but no cases occurred in the experimental group receiving B_6 as well as isoniazid during a ten-week period. The mechanism of action is not yet clear, but if subsequent trials prove equally successful, a new use for B_6 will have been established.

Another illustrative problem is the role of vitamin C in the metabolism of extrinsic drugs. Two converging lines of study by Brodie and associates at the National Institutes of Health may be illuminating. The abundant excretion of ascorbic acid from rats receiving various drugs, as previously shown by King, was found in Brodie's laboratory to result from biosynthesis of the vitamin. Hence, it seemed to play an active part. Further experiments revealed that guinea pigs, when deprived of ascorbic acid, metabolize aromatic drugs slowly, but regain their normal rate when the vitamin is again administered.

To the biochemist, this effect was striking in that a variety of aromatic drugs are apparently metabolized by chemical reactions in which the vitamin is a common denominator. Reinforcing this possibility was the discovery of a test-tube reaction, nonenzymatic, in which such drugs are oxidized in the aromatic ring just as they are metabolically. Ascorbic acid, oxygen, an iron salt, and the chelating agent Versine, when added to aniline, for example, yielded para-aminophenol.

The science of nutrition now occupies a position

From a paper delivered at the Bicentennial Conference, Columbia University College of Pharmacy, New York, October 14, 1954.

roughly analogous to that of microbiology. Just as the major infectious diseases have been controlled, so the specific deficiency diseases have yielded to research and a concerted attack. In both cases, this has freed scientists to work on other problems, many of which have grown in importance as more people live into later years. Far from reaching the point of diminishing returns, nutrition research today promises unprecedented advances.

Before examining new problems in this field, I should like to mention the need to continue the improvement of foods, food habits, and evaluation of nutritional status. Despite the adequacy of the usual American diet, many persons may be in a borderland state with regard to nutrition. Although resisting overt deficiencies, they may suffer suboptimal health and be unprepared to withstand a temporary dietary imbalance or the stress of disease. Methods for evaluating nutritional status are sought, so that the exact nature and magnitude of this problem can be determined.

in Nutrition

By W. H. Sebrell, Jr., DIRECTOR NATIONAL INSTITUTES OF HEALTH, PUBLIC HEALTH SERVICE U. S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

Nutrition in the Chronic Diseases

Before World War II, major trends were apparent in the Nation's health. Sanitation, better nutrition, and improved medical treatment had all contributed to longer life; and more people were subject to the ills of an aging population—the so-called chronic diseases. Emphasis in medical research has shifted to those problems—arteriosclerosis, cancer, arthritis, neurological disorders, diabetes and others. In this process the science of nutrition has been extended. The early workers defined our needs for various nutrients and then turned their attention to means of application. Today, an understanding of why nutrients are required —how they are used by the body—is essential and not beyond reach.

Nutritionists are investigating the complex processes of tissue growth, organization, function, senescence and death—in a word, metabolism. This has become the principal frontier of nutrition science, and many facts pertaining to the chronic diseases are emerging in its development.

Obesity.—An important but little understood link between nutrition and chronic disease is obesity—a serious disorder called sharply to attention by actuarial experience, and now investigated in several laboratories. About a quarter of the adult population is sufficiently overweight to impair health. Mortality for this group, according to estimates by Metropolitan Life, is well above normal at every age and rises with increasing weight. Obesity is associated with high mortality from cardiovascular-renal disease, diabetes, liver disease, and childbirth. Deaths from diabetes are more than three times as common in the obese as in persons of average weight, and deaths from liver cirrhosis among men, more than twice as common. The overweight also have a high incidence of hernia, urinary impairments, cancer of the endometrium, and gout. More than thirty years ago, Joslin stated: What the thermometer is to acute illness, the scales are to chronic disease.

Most authorities believe that obesity, in the vast majority of cases, represents merely an excessive appetite, rather than a metabolic aberration such as hypothyroidism. Apparently the normal person possesses some kind of mechanism—probably involving the hypothalamus—for balancing appetite against the body's needs. This mechanism, termed by Jolliffe the "appestat," fails to synchronize in the obese; but the reason for its failure is unknown. Is it disrupted psychologically or physiologically? The problem is fertile for research.

The fact that obesity is correlated with certain chronic diseases does not establish a causal relation. Unknown etiologic factors may be common to these conditions. In various studies, however, caloric restriction has prevented cancer in mice, prolonged greatly the life of rats, and reduced the signs of diabetes and hypertension in humans. Moreover, striking decreases in the incidence and severity of diabetes and hypertension accompanied loss of weight in Europe during both World Wars.

For the present, those who undertake to lose weight should bear in mind two points regarding specific nutrients. First, obesity is due simply to overeating in terms of total calories: the source of the calories—whether carbohydrate, fat or protein—is apparently immaterial. A martini cocktail in excess of energy requirements is just about as fattening as a doughnut or a two-inch portion of custard pie. Secondly, in reducing the caloric intake, one should be especially careful to prevent deficiencies of vitamins, minerals and proteins, by observing closely the diatary balance or by daily supplementation.

Atherosclerosis.—The subject of obesity provides a point of transition to the role of fat metabolism in the

development of cardiovascular disease: Research on atherosclerosis, the principal form of arterial degeneration, is proceeding along many lines. Most investigators, though, work from the hypothesis that the body's fat-handling system plays an etiologic role. Deposited cholesterol, a fat-like substance, contributes to the arterial thickening that characterizes the disorder. Moreover, some animals on high-cholesterol diets develop arterial lesions, and abnormal cholesterol-bearing molecules have been found in the blood of sclerotic patients.

Observations on patients after weight reduction have shown a decline in circulating cholesterol of the type suspected in this condition. To what extent the lower level is due to reduced fat ingestion rather than reduction of weight has not been determined.

Anfinsen and others at the National Institutes of Health have identified a "clearing factor," which diminishes the cloudiness of blood occurring after a fatty meal. The factor is an enzyme elicited by injections of heparin or, in recent studies using rats, by oral administration of silicotungstate and other simple mineral compounds. In normal persons the blood clears automatically within a few hours, but in others the cloudiness persists, possibly leading to atherosclerosis. The clearing factor not only eliminates the cloudiness, but appears to break down the suspected cholesterol-bearing molecules.

The fact, however, that the body readily synthesizes cholesterol from simple, ever-present substances compels caution. B vitamins, amino acids, and other nutrients are involved in cholesterol metabolism, and various nutritional deficiencies affect its deposition. We do not yet know, for that matter, whether the dietary level of the substance is of practical significance. For persons with atherosclerosis, the best diet known is a normal balanced one, unless complications indicating a special diet are present.

Epilepsy.—I believe you will be interested in current research on the role of another nutrient, an amino acid, in epilepsy. Biochemical studies by Tower, now at NIH, indicated that epileptic tissue is metabolically defective—principally in its capacity to maintain glutamic acid. This amino acid contributes to the protein structure of the cells, to their energy supply, and to their utilization of potassium. Tower induced the metabolic defect in animals, and then administered two compounds in large doses—glutamine (the amide of glutamic acid) and a closely related substance, asparagine. Both alleviated the abnormalities without affecting normal tissue. Next, studies on patients with intractable seizures were undertaken in our Clinical Center.

Two types of study are being conducted. Electroencephalograms are evaluated during intravenous infusion of glutamine or asparagine, and patients receiving daily oral doses of asparagine are observed over extended periods. With both approaches, significant improvement has been noted. During prolonged asparagine dosage, definitely fewer seizures occurred in several cases. This in no sense implies a cure: if asparagine or glutamine proves in further trials to be of practical value, regular and permanent dosage will probably be necessary. Results to date establish the basis for a better understanding of epilepsy and a rational approach to its treatment.

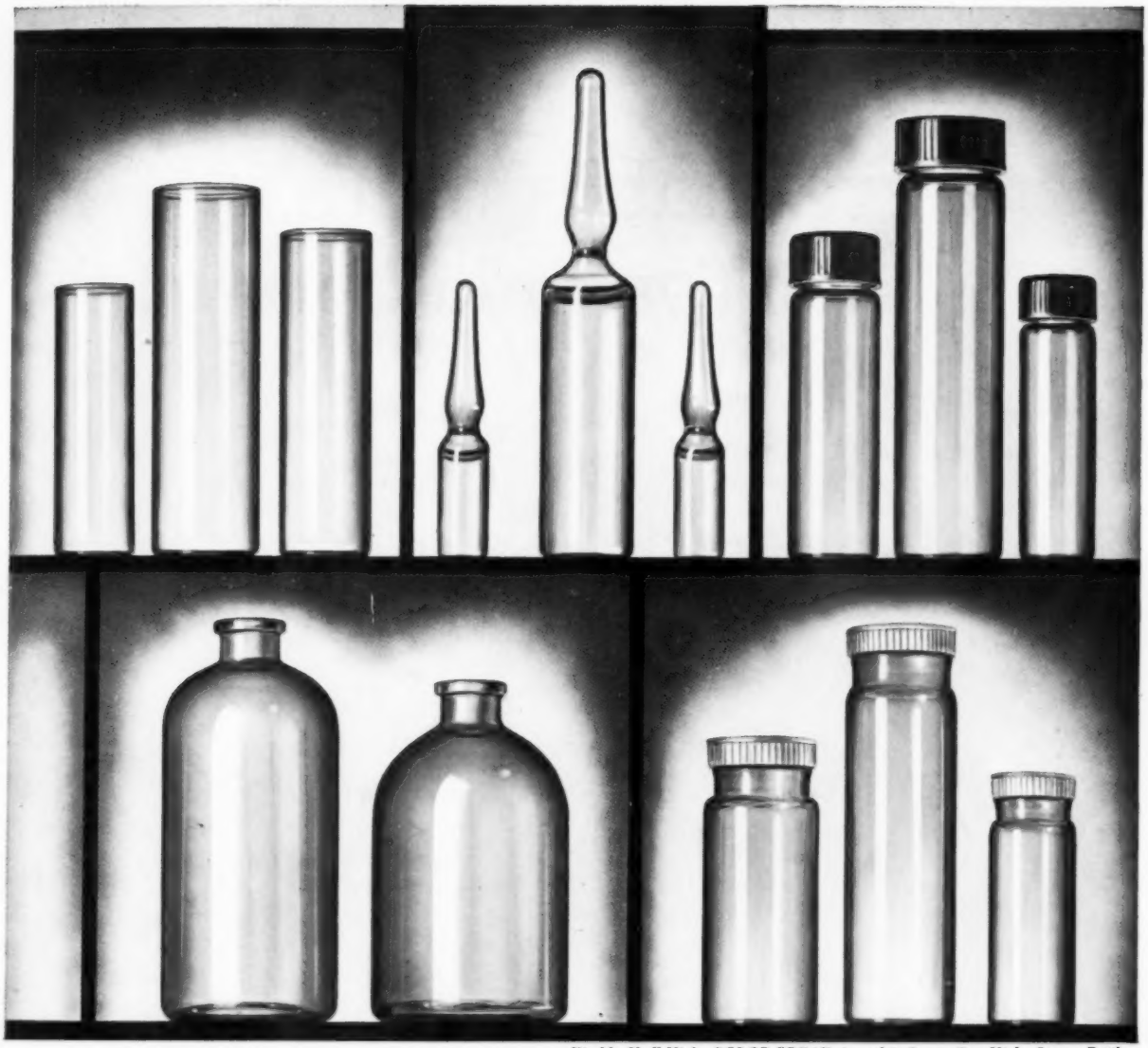
Metabolic Studies.—The relation of certain nutrients to the functions of the adrenal cortex is a subject of mounting interest in various health problems, such as stress and rheumatoid arthritis. A rapid decline in the ascorbic acid and cholesterol of the adrenals is associated with increased secretion of adrenal cortical hormones, suggesting a role of these substances in hormone production. The question naturally follows as to whether a deficiency of the vitamin, ascorbic acid, would diminish adreno-cortical excretion. On the contrary, studies with scorbutic animals, by Done and others, revealed elevated steroid levels in the blood, and when ascorbic acid was administered, the levels fell. Does this mean that the vitamin deficiency increased the liberation of hormone? Or did it interfere with its use or loss? The exact role of ascorbic acid with respect to adrenal activity remains to be defined.

A further illustration of the challenging problem of metabolism and chronic disease concerns the relation of the adrenals to one of the B vitamins, pantothenic acid. This is an active principle of coenzyme A and plays a key role in cellular oxidation. Pantothenic acid deficiency in experimental animals may result in lesions of the nervous system, impaired leukocyte production, gray hair, and adrenocortical deterioration. The adrenals are further damaged by treatment with ACTH, as though they could not withstand the stimulating effect. The function of the vitamin in human nutrition has not been determined, but recent studies suggest an important part in the reaction to stress. Ralli reports that calcium pantothenate in large doses influenced some of the blood and urinary findings elicited by voluntary immersion of men in cold water.

One such change was elevated blood levels of ascorbic acid. Without attempting to interpret this, I mention it to illustrate the complex inter-relation of nutrients. Data on such interrelations are also manifold in the study of trace elements. It is known, for instance, that excessive traces of molybdenum in soil may create in foraging livestock a high demand for copper, which is needed for the utilization of iron in blood and enzyme formation. Recent investigations have extended knowledge of the interdependence of copper, iron and cobalt. In other studies, interrelations have been established between choline and the vitamins B_{12}, folic acid, and ascorbic acid; and these have been related to the amino acids cystine, methionine, tyrosine and phenylalanine.

Research in metabolism, though often applied to a specific health problem, is gradually building toward an over-all view of body chemistry. Stated in another way, biological science is seeking to explain the mechanisms of nutrition—to map the interrelations of nutrients,

(*Continued on page 705*)



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GLASS AEROSOLS* for Pharmaceuticals

by Francis A. Mina, Ph.D.

TECHNICAL DIRECTOR,
ZONITE PRODUCTS CORPORATION, NEW BRUNSWICK, N. J.

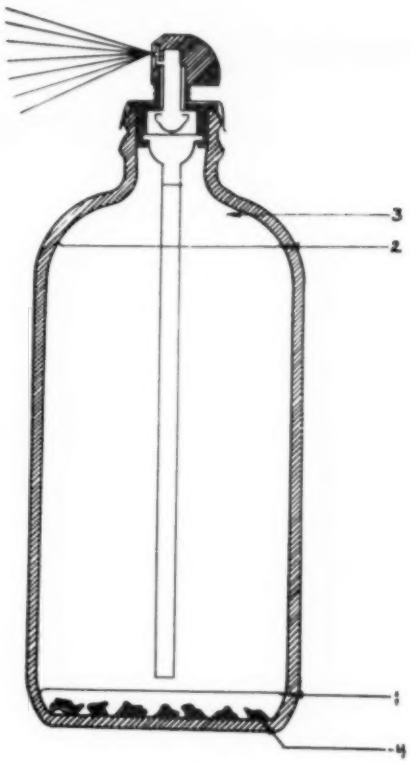

Fig. 1

It is not unlikely that the meteoric rise of the Aerosol industry to its present day position is unique in the various fields of commercial endeavor. Certainly, one reason for such success lies in the innate desire of the general public to do a particular job efficiently, and with as little effort as is practicable. While cost is always a primary consideration, it is apparent that generally it does not take precedence over that of convenience, within reasonable bounds.

Until recently, "push-button" convenience and efficacy offered by conventional aerosol packages have had certain limitations in practical application, the chief limiting factor being corrosion of metal cans.

The pharmaceutical industry, particularly, was also faced with the problem that certain potentially useful products could not be satisfactorily packaged in metal because of undesirable reactions of product components with protective internal can coatings currently available. Thus, from an early date, it was apparent to the aerosol industry that the ultimate answer to these difficulties would lie in packaging such products in containers other than metal cans.

Probably no segment of business is more aware of the advantages of glass packaging than is the pharmaceutical industry. Certainly, the most important feature of glass is its inertness to most materials. Other distinct advantages are product visibility, sparkling attractiveness, and an almost endless variety of designs. These factors, along with the exclusion of air, with its attendant risk of oxidation to many sensitive ingredients, further potentiates the importance of glass aerosols for pharmaceuticals.

Fig. 2

The general utilization of glass in the packaging of self-dispensing pressurized products first was made practical by the introduction of the *three-phase principle* for dispensing aqueous-based products,[1] and by the Ultra-Low Pressure System for dispensing alcohol-based products[2]. Patents have been applied for on both these developments. While not restricted to choice of propellents, both developments produced sprays of satisfactory fineness, utilizing pressures as low as 11 to 15 p.s.i.g. at ordinary room temperatures. Even lower pressures can be used satisfactorily with a specially designed valve expected to be marketed soon.

A brief explanation of the principles involved in these developments will help to illustrate the applicability of either system to many uses.

In general, the three-phase system (Fig. 1) is designed for dispensing solutions which are relatively immiscible with the propellent. In this system the propellent "1" remains at the bottom in the form of a distinct layer or pool. The product "2" contained in the package, not being

*Delivered at the 16th Annual Packaging Forum, October 26, 1954.

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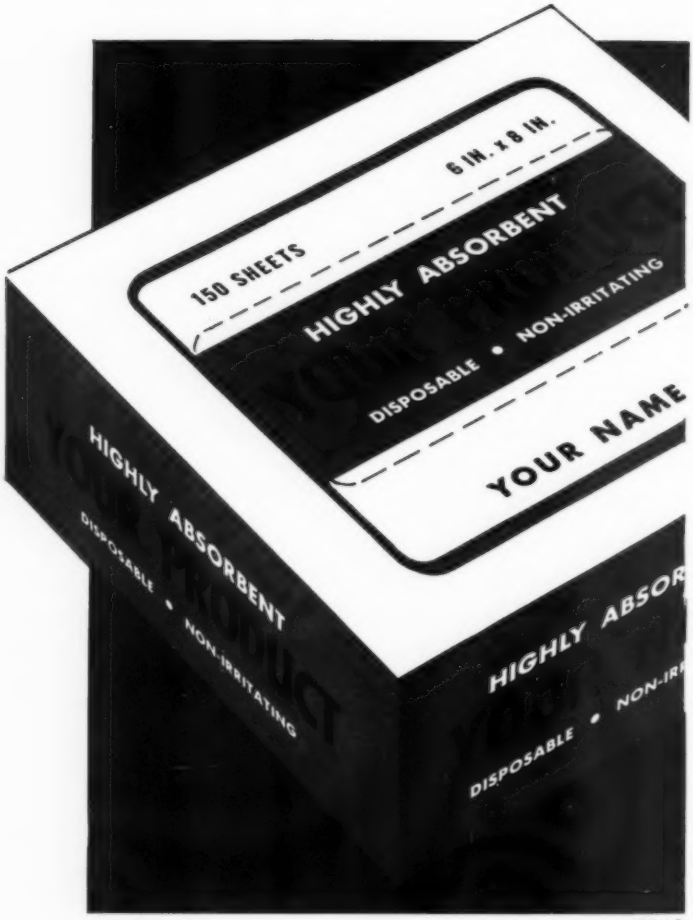

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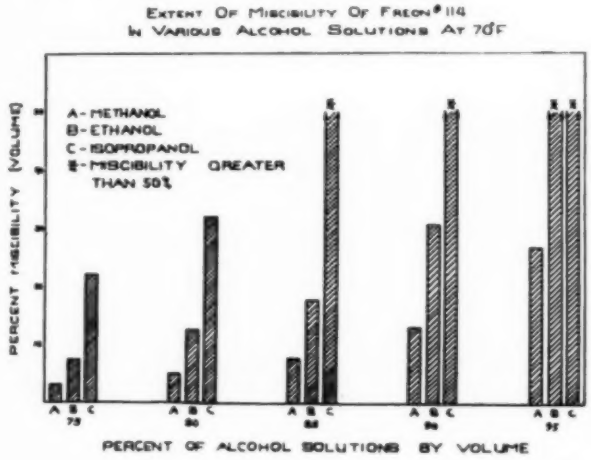
miscible with the propellent, is sprayed without dilution by means of the pressure exerted on such liquid by the propellent vapor "3." As the product is sprayed, the head space is increased with a resulting decrease in the pressure exerted by the propellent vapor. This decrease in pressure allows a "boiling off" of the propellent reservoir until the vapor phase reaches equilibrium, in accordance with the pressure-temperature relationship of the particular propellent, or propellent combination, used. The presence of the "boiling stones" activator "4" minimizes the lag phase of pressure build-up normally encountered during prolonged spraying. The use of


EXTENT OF MISCIBILITY OF FREON® 114
IN VARIOUS ALCOHOL SOLUTIONS AT 70°F
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PERCENT MISCIBILITY (VOLUME)
PERCENT OF ALCOHOL SOLUTIONS BY VOLUME

Fig. 3

such activator allows the complete contents of the unit to be sprayed with relatively uniform pressure and spray pattern.

Figure 2 illustrates the commercial application of the three-phase system, showing the component parts.

The Ultra-Low Pressure System for dispensing products containing relatively high concentrations of alcohol is predicated on our finding that fine atomization of spray delivery is effected by factors other than pressure alone. We have found that a misty spray of alcohol-based products can be achieved by approximately saturating certain concentrations of aqueous solutions of aliphatic alcohols. The presence of water in the alcohol-based product markedly reduces the extent of miscibility of propellent, and within certain carefully controlled proportions and use of suitable propellent or combination of propellents, it is feasible to obtain fine mist delivery of product, using as little as approximately 10 per cent by volume of propellent.

Propellent

While any of the commonly available propellents, or combinations thereof, can be utilized, a number of factors dictate the major use of dichlorotetrafluoroethane as the propellent of choice. Among these are:

1) *Low order of toxicity and irritation.* This is of especial importance for dispensing products designed for application to living tissues. Dichlorotetrafluoro-

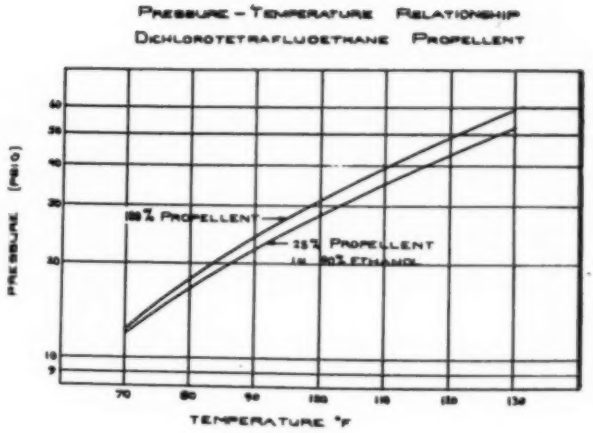

Fig. 4

ethane is classified in Group 6 by Underwriters Laboratories. To this group belong the least toxic of the commonly used propellents.

2) *Limited miscibility.* Its limited miscibility in aqueous solutions of aliphatic alcohols allows relatively small proportion of propellent to be used with resulting fine atomization of product. Figure 3 shows the extent of miscibility of dichlorotetrafluoroethane in aqueous solutions of aliphatic alcohols of various concentrations at 70° F. For example: at this temperature, only five per cent of propellent is required to saturate an 80 per cent solution of methanol, while similar concentrations of ethanol and isopropanol require only 12.5 per cent and 36 per cent by volume respectively to achieve saturation.

Note that the degree of miscibility is related directly to the number of carbon atoms in the aliphatic alcohols.

3) *Stability.* A wide range of products containing soaps, detergents, essential oils, and many ingredients commonly used in pharmaceuticals have been found to display remarkable stability in contact with dichlorotetrafluoroethane.

4) *Pressure.* The pressure-temperature relationship curve of dichlorotetrafluoroethane (Fig. 4) shows that at 70° F. the propellent produces a gauge pressure of approximately 13 pounds, increasing gradually to 59

(*Continued on page 682*)

Fig. 5

When the door is opened

our tailor-made packages begin to

SING

Containers for many products are discarded after one use. But your proprietary products have to live in their containers for weeks or even months. Every time the product is taken from the bathroom cabinet or dressing table, the package can please—or disappoint. Continental takes infinite pains to see that its lithographed metal containers for toiletries and powders *always* please. They're good to look at, easy to use, and their protection *lasts*. For a tailor-made package for your product—and tailor-made delivery, engineering and research to match—call on Continental.

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Packaging and Selling

Good Taste

According to a flavor panel held during the recent meeting of the American Chemical Society, the human tongue is a pretty sensitive instrument and, in many cases, superior to anything that can be found in the laboratory.

Of course this is not a revolutionary theory because it has long been held so in tea and coffee tasting and in the brewery business as well as in many other fields. We remember many years ago when the Norwegian cod liver oil exporter, Isdahl, challenged the methods of analysis used by the Appraiser Stores in New York to detect adulteration in cod liver oils. Isdahl stated that he could detect by taste the mixture and amount of other fish oils with cod liver oils far better than anything detected by instruments or chemical tests. Isdahl then went on to prove that he could do this in a cod liver oil chewing contest which baffled the chemists at the Appraisers' Stores.

For these reasons, we don't know just what they meant when some of our good friends on this panel talked about a bold, adventurous new theory of taste coming into the laboratory. On this panel was Dr. Arthur L. Fox of the Colgate-Palmolive Co., Dr. Robert L. Warfield of the Bristol-Myers Company and Dr. Hubert L. Frings, Pennsylvania State University.

According to Dr. Fox, there are ten classifications of taste and four of these classes include about 76 per cent of the U. S. population. These four, according to Dr. Fox, are "bitter-salty," "tasteless-salty," "bitter-sweet" and "tasteless."

After hearing these classifications, we are in full accord with the fact that the tongue is infinitely superior to the instrument.

Dr. Frings, who is Professor of Zoology at Penn State, said that he has learned a great deal about taste from roaches, caterpillars, rabbits, quail and as a further thought, man.

We would like to suggest to Dr. Frings that he add to his research the Japanese beetle.

We ourselves have for several years conducted a very intensive research on the Japanese Beetle, having picked conservatively over a million beetles from the leaves of our garden plants and dumped them into a kerosene can, in addition to using every possible kind of a spray.

As anyone who has ever hunted the Japanese beetle knows, that unutterably vile insect has strong taste preferences. For instance, the Japanese beetle will fly over a wide assortment of choice and variety of foliage to spot a grape leaf, a pussy willow leaf or a raspberry leaf. This offensive insect has a very discriminating taste for roses, going into ecstacies over certain of the tea roses and almost ignoring certain of the polyanthers. They will almost defoliate the leaves of certain Rugosa roses, and completely ignore the leaves of many other rose varieties.

It seems to us that there is a fertile field for flavor or taste investigation in the eating habits of this despicable insect.

We should like to suggest several lines that taste or flavor research could take. The first project, we would guess, would be to find out why this depraved bug has such a ravenous craving for one flower or one variety of a flower and for a limited number of leaves that it will spend its entire life on this one diet. This is contrary to the flavor habits of human beings and most animals, in that any taste endlessly repeated brings a state of revulsion.

The second thing we would like to know is whether in these particular flowers and leaves which are selected, there is some chemical factor necessary for their own peculiar dietary system that overrides the flavor factor.

Everywhere in the insect world, there are interesting and curious cases of highly specialized feeding. This is particularly true in the insects which feed upon economic crops, where a high degree of specialization takes place almost to the point of extinction of the insect if this one feeding medium is not available. The silkworm with mulberry leaves and cotton boll weevil are only two of many instances.

We ought to know whether this highly specialized feeding is a habit characteristic based upon some biological necessity, whether there is some inherited nutritive factor or whether it is simply a case of highly developed flavor specialization and preference.

Record for Home Instruction

Anyone who buys a new Bendix washing machine will also get a phonograph record with full instructions on operating this machine.

We think this is a wonderful idea, which could have much broader applications. In this day of increasing self-service selling and increasing technical complications the buyer needs plenty of help. It seems to us the phonograph record lends itself to home demonstration and explanation in an unusually happy way.

Probably in applying this method of directions for use some bright lad will come up with the idea of putting

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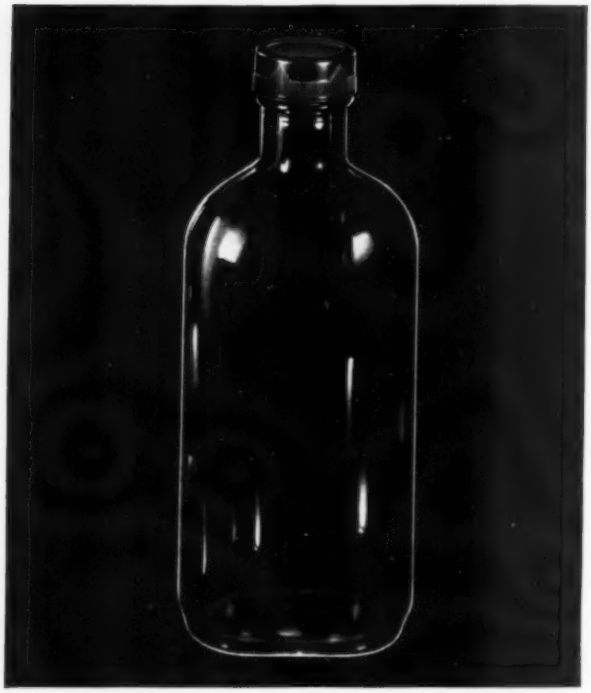
...BUT ALL ANCHORGLASS CONTAINERS HAVE THE SAME QUALITIES

THEY are uniformly strong, tough, dependable lightweight glass containers—high in chemical durability, accurate in dimensions, capacity and finish. They are designed to withstand the knocks of modern high speed production lines, handling and transportation.

Anchorglass containers are the result of practical engineered designs, careful selection and control of raw materials, uniform distribution of glass, precise temperature control in annealing and thorough quality control through laboratory tests and regular inspections.

If you package or contemplate packaging in glass let us send you sample containers with suitable closures for your particular needs. The services of our Package Engineering and Research Laboratories are also available to help you solve glass packaging problems.



Anchorglass® Narrow Mouth Ovals are available in 6, 8, 16 and 32 ounce sizes, in crystal and amber glass. They are ideal, economical containers for alcohol and many other liquid products.

ANCHOR HOCKING

GLASS CORPORATION
LANCASTER, OHIO

★

The Most Famous Name in Glass

something popular on the other side which will at least guarantee preservation of the business side.

Growing Drug Self-Service

According to reports from the Associated Chain Drug Stores self-service chain stores now number 650 stores of this kind and may number between five to six thousand by 1960.

Trade Work

You have to be quick on the trigger if you want to trade mark a word that has the elements of popular acceptance as a descriptive term.
An apparel company has just lost an appeal in an attempt to trade mark the word "pre-teens."

Packaging Dilemma

According to a study of self-service operations, one of the fundamental purposes of packaging is to decrease pilferage and prevent damage to the merchandise. However, according to an expert, the value of packaging in any self-service operation is subject to at least one important consideration: "Is anything accomplished by taking merchandise out from underneath glass and putting it back under cellophane? With very few exceptions, customers wish to touch the fabric before they buy soft goods."

The Package and Distribution

The package may play a greater part than has been expected in determining or classifying distribution.
The cosmetic industry, or at least a number of its larger members, has been straddling different classes of distribution where totally different problems are involved, such as pricing, discounts, display and in other ways. Now we hear a variety of complaints arising out of the self-service grocery store field and also from some of the variety stores that are going into self-service that their method of doing business requires special packaging.
It is becoming increasingly evident that in self-service display a package must be capable of very rough handling that will enable it to stand up against soilage as well as mutilation or breakage. This of course is not a particular problem in personal selling, especially in drugstores and department stores.
Self-service packages must increasingly do the entire job of selling and answering questions through informative labels. Crowding all this information on the label may mean a compromise with attractive appearance that is not necessary in personal selling.
The problem of theft does not enter into personal selling but is a serious question which must be considered nationally by the packaging people in self-service.
It may become necessary in self-selling to stamp with a great deal more prominence such factors as price, quality and any cautions that might be necessary. This problem in stamping might affect the beauty of the package in a way that might not be acceptable for cosmetic products in a department store.
There are so many compromises becoming necessary for the package, that is, in advertising, such as the color limitations and type visibility, in television, in materials handling which may become a tremendous factor in retailing in the future, in the different kinds of displays, that is, counter, shelf and rack, that are developing in different types of stores, and in the problem of personal selling as opposed to impersonal selling that it is quite possible that certain changes may become necessary in a package in each broad classification of distribution.

Ribbons for Rats

Pioneer research often has to travel down strange and devious paths, at least it seems so to the layman. These research paths often seem very, very strange.
For instance, here is a picture of a Colgate researcher brushing a rat's teeth with a dentifrice containing Gardol—sodium N—lauroyl sarcosinate—with a radioactive isotope in it. The tooth brushing was done with a tiny mascara brush and, contrary to the treatment given to small children, the rat was anesthetized so that it wouldn't struggle against the brushing.
These rat experiments are being made to prove that Gardol, the anti-decay ingredient of Colgate Dental Cream, has a long-lasting effect because it remains in the mouth for at least forty-eight hours.

Gift Package Failures

When a gift package fails to click, one of the biggest reasons is an attempt to force an after-use that is not related to the product. This is an opinion expressed by Milton Weill, President of Arrow Manufacturing Company, in a talk to the Merchandising Executives Club of New York.
Mr. Weill then went on to say, "If the after-use is logical, and does not impede a straightforward presentation of the merchandise, it may be a value plus."
It seems to us that Mr. Weill is putting his finger on a situation that is involving quite a few people today.
The liquor people have been tumbling headlong into fancy containers. Not content with involving themselves in some of the difficulties of the perfume industry, these people, in addition to giving this fancy container for free, are now getting involved in a lot of after-use conversation.
These fancy decanters are unquestionably bringing in some additional business in gift purchases to the liquor

people. If they could stop there and restrict the fancy container to a seasonal gift package, there would seem to be plenty of justification, but probably, before they know it, some ambitious plunger in the distilling business will be making a fancy decanter an all-around-the-year package.

As for the after-use, one leading distiller who has recently brought out a very attractive decanter is talking about it for table lamps, table legs and an odd assortment of after-uses. What Mr. Weill means is that no matter where this after-use appears, it will always be to everybody still a whiskey bottle.

We notice that a Philadelphia company is packaging Virginia-style hams in corrugated containers fashioned like log cabins. These log cabins, which have an after-use as a toy, has boosted these ham sales 43 per cent, according to company reports.

We think a ham and a log cabin is a cute idea and a novelty that will temporarily appeal to children. But it will still be to everyone that sees it, a package that held a ham. If it does not look like a package that should hold a ham, then maybe this initial novelty of appearance won't work out quite so well in the long run.

Some Bull

Ankonian is a black Angus bull who made the headlines when he was treated for pneumonia in a cellophane oxygen tent. In around-the-clock nursing, the big black fellow used up six $15.00 tanks of oxygen a day and was liberally dosed with penicillin and aureomycin. Ankonian is supposed to be the first bull that ever got into an oxygen tent. The reason for this is that he is valued at $50,000, is one of two bulls in a herd of 300 cattle and is expected to sire 1,000 calves a year.

Hair Tonic Deal

Jeris Hair Tonic has a combination deal with a pocket wallet using a folding carton boot to hold both the separately packaged tonic and the wallet in such a way as to give full display to both items while taking little counter space. A special lock in the boot not only holds the wallet firmly in position but makes it pilfer-proof.

The boot keeps the tonic and the wallet in a permanent unit for shipping and display space. Cartons are designed and made by Robert Gair Company, Inc. and A. R. Winarick Inc. of New Brunswick, N. J.

Ways to Meet Discounts

A professor of Political Science at the University of California has just completed a study of discount houses and their technique. This professor comes up with the conclusion that discount houses owe their existence to fair trade laws. The professor has three recommendations for retail stores. (1) Demand that the makers enforce prices across the board or cut prices themselves. (2) Develop a line of private label merchandise. (3) Urge an investigation of alleged discount operators where in some cases tax advantages may be improperly allowed.

As a political scientist the professor missed one obvious addition to his list of remedies and that is for the store to cooperate as much as possible with franchise or selected distribution merchandise.

Does Competition Reduce Costs?

One of the constant sources of amazement to us in this exciting and colorful era of growing wealth and expansion is the way in which two fundamental social activities have been constantly moving in opposite directions. These two factors are the cost of production, which has consistently shown an annual decrease, and the cost of distribution, which has consistently shown an annual increase.

One of the outstanding phenomena of human achievement is the way in which the cost of producing food products has decreased over this last generation. Theoretically, food today should be so cheap that it would hardly be a factor in living costs. Unfortunately, both political considerations as well as increasing cost of distribution have brought about the opposite condition, making food a very substantial and increasing part of the cost of living.

In a recent article in the Journal of Commerce, in the Fall Grocery Marketing Section, J. A. Logan, President, National Association of Food Chains, makes the following statement: "The present volume of free deals, coupons and giveaways is probably unprecedented in the history of the food business. Use of stamps and other premium systems by retailers to attract business has been another indicator of growing competition in the always competitive food industry."

Emphasis on "extra" services and "extra" inducements to customers, coming at a time when farm prices are dropping focuses attention on the cost of all these competitive efforts.

Mr. Logan then asked the question, "Are the costs of all the added services and inducements to the customer really justified by the demonstrated acceptance? Can the public afford the luxury of permanently adding these costs to food prices?"

A few years ago, self-service and the super-market were hailed by businessmen as a new era in reduced costs of distribution. It was then fondly believed that mechan-

New beauty... New safety

WHEATON GLASS-LINED PLASTIC BOTTLES

A few months ago the news first went around: Wheaton has developed glass-lined plastic bottles strong enough to use as aerosol containers!

Packagers saw in them new beauty, new safety, exciting new sales appeal. The carnival of colorful bottles already on the market is evidence of their immediate success.

Here are design possibilities irresistible to the sales-minded packaging engineer. For these bottles can be custom-molded, and the color range is as wide as that of plastic and glass together. And there's a choice among clear, translucent or opaque coatings.

Here is real safety, too. For if the glass is broken, the tough plastic skin prevents the escape of glass splinters.

Wheaton glass-lined plastic bottles are the ideal packaging for superb cosmetics (and scores of other products). Actually, these bottles have so many useful applications we don't profess to know them all ourselves. Let us explore with you the full advantages they can offer to *your* products.

WHEATON PLASTICS CO.
MAYS LANDING, N. J.

Wheaton has made fine glass bottles since 1888

SHEFFIELD TUBES

with McKESSON & ROBBINS' TAWN...the brush is purely ornamental

Yes, the brush is old...
and purely ornamental. Popular Tawn Brushless Shave is new...and efficiently serves the comfort of modern men.
Two such established firms as Sheffield Tube and McKesson & Robbins, Inc., are old hands at turning their experience into new packaging concepts that make pleasant music on the cash register!
For collapsible tubes better designed to sell and protect, try Sheffield Process Tubes on your next order.

THE SHEFFIELD TUBE CORPORATION

Factory and Home Office: New London, Connecticut • Sales Offices: New York • Chicago • Los Angeles

ization, which had wrought so many miracles in cost reduction in the factory, would now be introduced into the distribution in this new era of mechanized distribution. Apparently, the super-markets have not been able to resist the flood of competitive pressure to add constantly new services to their operation, to expand into plush palaces and to meet what marketing people seem to think is a consistent consumer demand to pay more money for services.

Some day we are going to really have a factual investigation on the question, "Does competition increase costs?" We are not too sure that we would want to sit on such a debate.

Polyethylene Tube for Packaging

Bradley Container Corp., Maynard, Mass., held a press luncheon last month to announce the first broad commercial production in this country of a polyethylene tube for packaging a wide range of drugs, foods, chemicals, cosmetics, novelties and industrial and other products. Bradley Dewey, founder and president of the 10-month-old company, stated that the firm is now in a position to supply polyethylene collapsible tubes and "squeeze-to-use" bottles in volume for those powders, liquids or semi-solids which are packageable in polyethylene.

The new Bracon tubes, as they are called, and bottles are produced by a patented extrusion-fabrication process, invented in Europe, to which Bradley Container holds exclusive rights for the United States and Canada. They combine the functional aspects of the squeeze bottle with the lower costs of metal tubes, while overcoming many of the drawbacks of both.

Eye droplets being applied in new one-drop Bracon polyethylene tube. Gentle pressure releases a single drop at a time.

The Bradley process includes offset printing in multicolors with exceptionally fine registration that helps to merchandise products sold in such competitive outlets as supermarkets, drug stores and variety stores. The containers have proved successful in Europe for packaging drugs, household chemicals, shampoos, shaving creams, shoepolish, syrups, mayonnaise and various spreads.

The tubes do not roll up, so that the product name is clearly visible at all times, constantly reminding the consumer what to repurchase when the need arises.

Most Bracon tubes cost slightly less than comparable tubes of aluminum and considerably less than the widely used tin tubes. Bracon tubes, moreover, are dentproof and hold their shape, for they easily recover from blows received in filling, handling and shipping. Since polyethylene is inert to most chemicals, the tubes are noncorrosive and eliminate the need for internal waxers or lacquers.

Pneumatic vacuum powder filler at Bradley Container Corp., filling Bracon squeeze-to-use polyethylene bottles with measured four ounces of bath talcum powder.

One of the great advantages of the tube is its controlled dispensing action, for each tube can be so constructed that it will (1) release one drop at a time, (2) release the entire contents in one application, (3) release a fine misty spray, (4) atomize powders, (5) release liquids like shampoos and detergents in pin-point streams, and (6) extrude semi-solids in various forms. Where required, the recovery of a Bracon tube helps to snuff back overflow, so the head remains clean.

Bradley's Maynard plant is now producing tubes and bottles at a rate of about 500 thousand a week and expects to quadruple that figure in a year. This firm is the first in the packaging industry to use a two-million-volt electron beam sterilization process for sterilizing both package and contents at the same time. This is accomplished at room temperatures so the plastic tubes and bottles will not melt or become deformed.

Darn Few One-Stop Shoppers

Another puncture has just been administered to a favorite theme of business orators in the last few years, that is, the one-stop shopper.

The School of Retailing, New York University has just completed a survey, gathered from one thousand persons who were charge account customers of the now defunct famous Loeser's of Brooklyn.

According to T. Dart Ellsworth, Director of Research for the School, "Credit customers made only slightly more than one in eleven of their total reported purchases. The tendency of people to shop around and their willingness to buy where they find what they want may prove an insurmountable obstacle for the one-stop shopping movement to overcome."

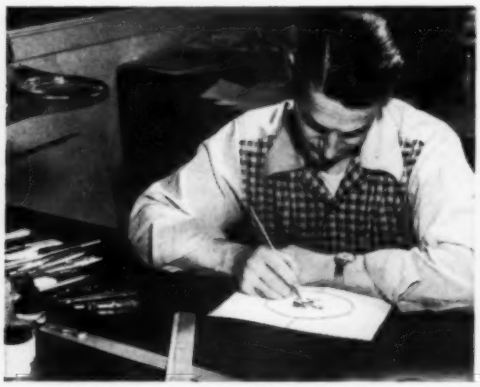
Minimum tightness of a cap is essential to avoid evaporation or leakage, whereas excessive tightness may make a closure difficult to remove. This spring torque tester tells how to adjust capping machines for the right amount of twist pressure for good sealing and easy removal.

Making closures that know how to sell your products

Blending function with sales appeal makes sales-minded closures—

SCIENTISTS, engineers, designers and marketing men are constantly working for you at the Duraglas Center—the world's largest glass container research laboratory. Here are some of the ways they determine the closure that's exactly right for your product...

How good is our tin plate? This instrument finds out. It measures the depth of draw of a specimen plate while another dial records amount of pressure it takes to rupture the plate.



Helping your package sell itself is the job of our engineer-artists. For example, food package designs convey cleanliness, while liquor salespackages suggest dignity and antiquity.

To study sealing problems we built this intricate instrument for detailed measurement of cap and glass finish dimensions. Cap or glass contours can be traced with a magnification of 25 to 1.

BEFORE:

On the left, an uninspired closure is the reason why this package is missing a golden opportunity to catch *extra* impulse sales.

AFTER:

On the right, now it's ready for self-selling! Bright, colorful closure-label combination makes this an outstanding, attention-getting salespackage.

METAL AND PLASTIC CLOSURES
AN (O) PRODUCT

OWENS-ILLINOIS
GENERAL OFFICES · TOLEDO 1, OHIO

Package Doin's . . .

Lozenge Display Package

Hynson, Westcott & Dunning have designed a new point-of-purchase display package for their Thantis Lozenges.

Nail-Polish Coating

Superior Products Co., 2200 South Lamar St., Dallas, is using the unusual merchandising technique of coating bottles with nail polish to make each container its own color chart. The nail-polish coating is the same as that which is packaged in the new bottle. Bottles and Empress plastic closures are supplied by Owens-Illinois Glass Co.

Six-Sided Vitamin Package

Vitaminerals, Inc., Glendale, Calif., is packaging vitamin tablets in a novel hexagonal folding carton designed and made by Angelus Paperbox Co. Two kinds of vitamin tablets are sealed in a long, wide ribbon of cellophane which, when rolled up, is in cylindrical form. A perforated slot in one of the six-side panels permits the ribbon of tablets to be withdrawn as used.

Plastic Adhesive

Adhesive Products Corp., 1660 Boone Ave., New York 60, has developed a new plastic adhesive, Polygriptex, which now makes it possible to stick ordinary paper labels to polyethylene squeeze bottles and polyethylene containers.

Jeweled Lipstick

Northam Warren Corp. has added a jeweled lipstick to its Cutex line. The lipstick is packaged in a unique display piece as an introductory feature, with each case fitted into the base of the card. There is a selection of attractive jewel designs on the lipstick caps made with "make believe" rubies, diamonds, sapphires and other jewels.

Pearlized Package

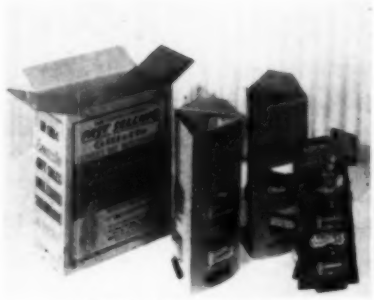
Browny of Honolulu is bringing out Momi Lani (meaning "Heavenly Pearl" in Hawaiian), a one-half dram of perfume. The package, made in their plant, is of polystyrene which has been drawn into molds, modeled after a real oyster pearl shell. The entire shell and base are hand pearlized. The company also made the acetate covers.

Special Razor Package

Gillette Safety Razor Co. has designed a new promotional package in order to sell a special Gillette Super Speed Razor set and bow tie combination for Father's Day. Triangular interior packing pieces, quickly folded into shape from flat sheets, assure protection for the pair of colorful displays. Die-cut holes accommodate the razor cases, and flanged tops prevent the unit from shifting when packed in the shipper. The package is made by Hinde & Dauch.

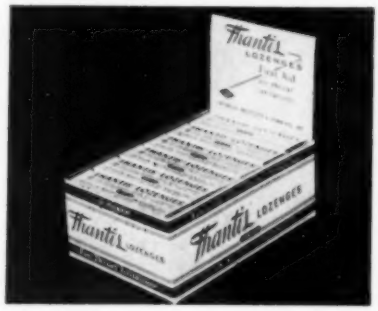
Cutex Jeweled Lipstick

Browny Pearlized Package

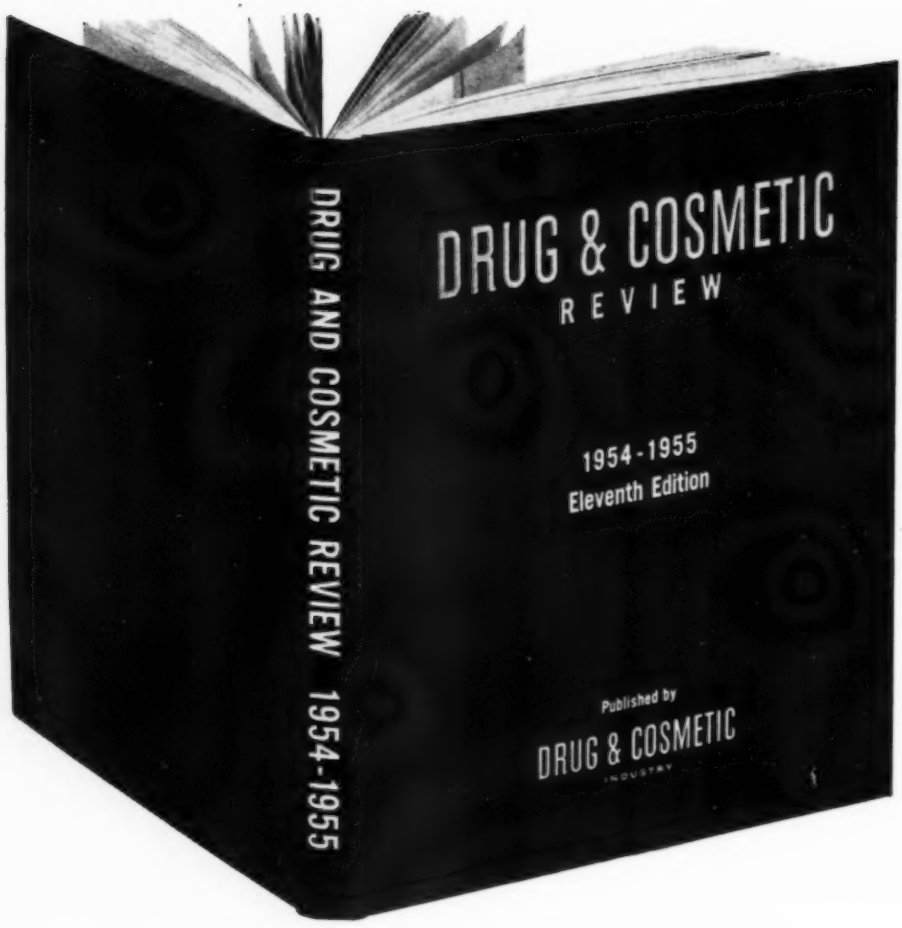

Gillette Safety Razor Package

Nail-Polish-Coated Bottles

Display Package for Lozenges



Hexagonal Vitamin Package



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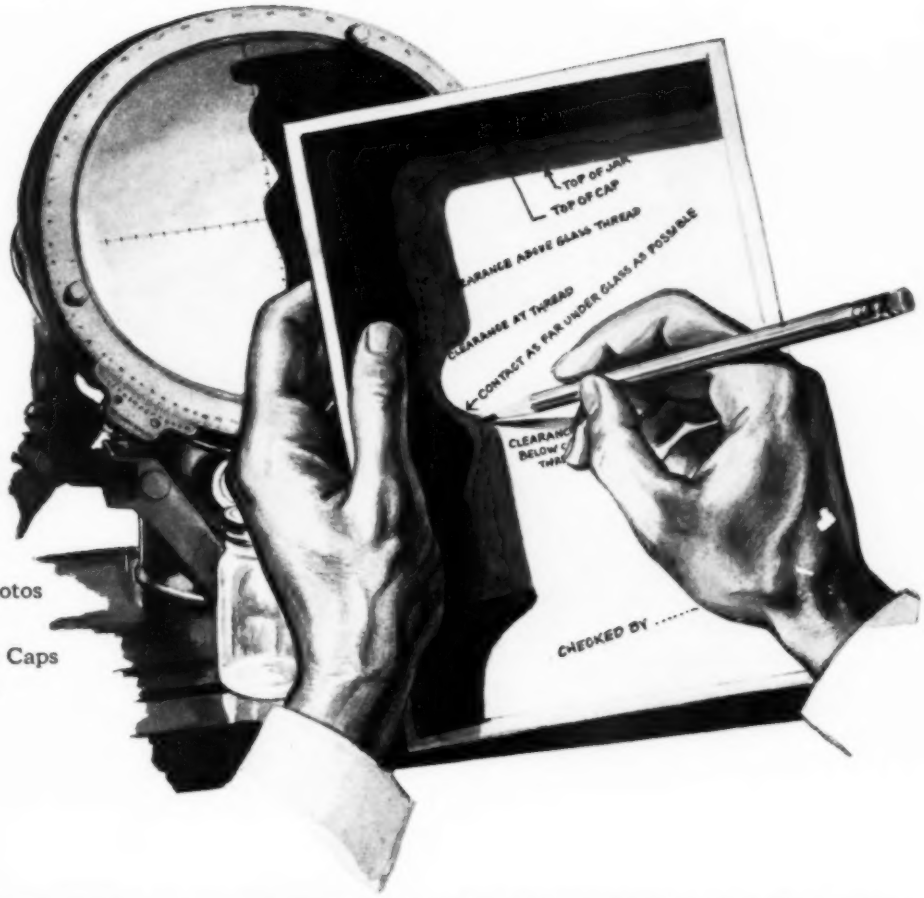

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Ball Technical Service is equally complete. It includes laboratory tests to select exactly the right materials for your product closures as well as field counsel on any filling-line problem. For metal screw caps, as for glass containers, *call* BALL *first of all.*

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Shapes up!

new, big market

Aerosol-packaged products formulated with "Freon"* propellents set the profit-making pace

No doubt about it—aerosol packaging offers you the chance to get into a big and booming market. Last year approximately 140 million aerosol units were produced, selling at retail for about $150 million. These figures show how completely people have taken to aerosols. Customers *know* an aerosol product will be clean and non-messy, easy to use, effective, convenient to buy and to store.

Study this wide-open market and see where you can profit from it. Your present products can take on new sales vitality in aerosol packaging. And the possibilities for new product development are practically unlimited.

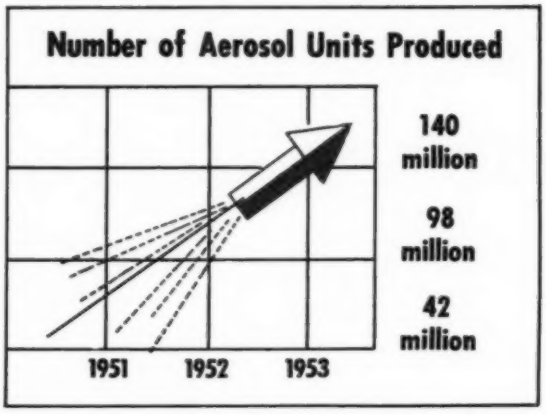
Here's why Du Pont can help you

Far and away most aerosol products get their "push" from a Du Pont "Freon" fluorinated hydrocarbon propellent. "Freon" propellents are nonflammable, nonexplosive and virtually nontoxic. Du Pont has accumulated years of experience in manufacturing these products . . . knows how they should be handled . . . and offers technical assistance to help you formulate aerosol products.

Here's how Du Pont can help you

You can take advantage of the knowledge of aerosol manufacture and marketing built up by Du Pont. Write for the interesting booklet "Package for Profit," or for specific market-research data. For this material—or for technical assistance of any sort—mail the coupon below today. E. I. du Pont de Nemours & Co. (Inc.), "Kinetic" Chemicals Division, Wilmington 98, Delaware.

THE AEROSOL SKYROCKET



Approximately 140 million units produced in 1953 —retail sales hit about $150 million

KINETIC

FREON

SAFE PROPELLENTS

*"*Freon" is Du Pont's registered trade-mark for its fluorinated hydrocarbon propellents*

DU PONT

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E. I. du Pont de Nemours & Co. (Inc.), Dept. D. C.
Room N-11500, Wilmington 98, Delaware.

☐ Send the booklet "Package for Profit."

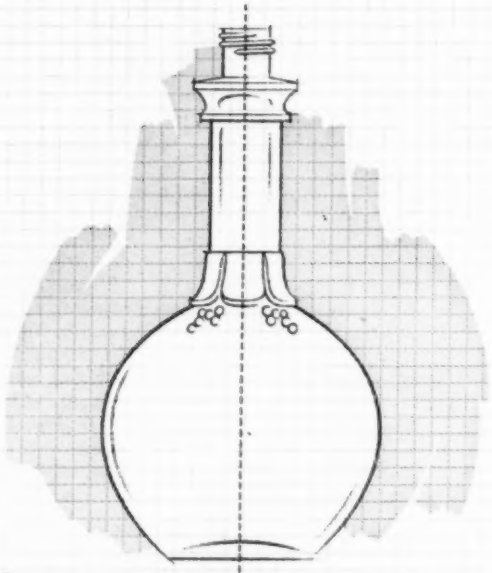
☐ Send market-research data.

☐ I am interested in technical assistance.

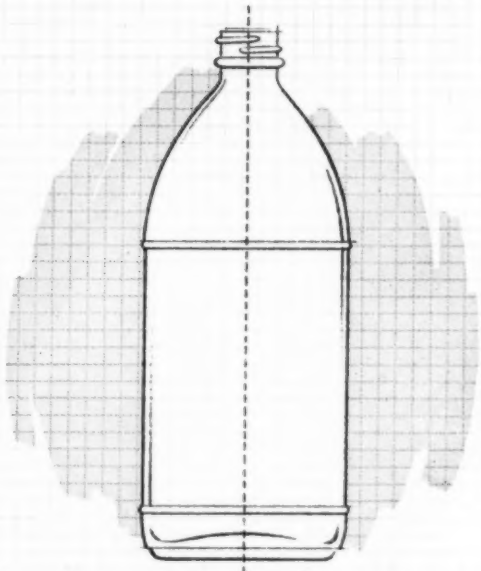
Name_____

Position_____

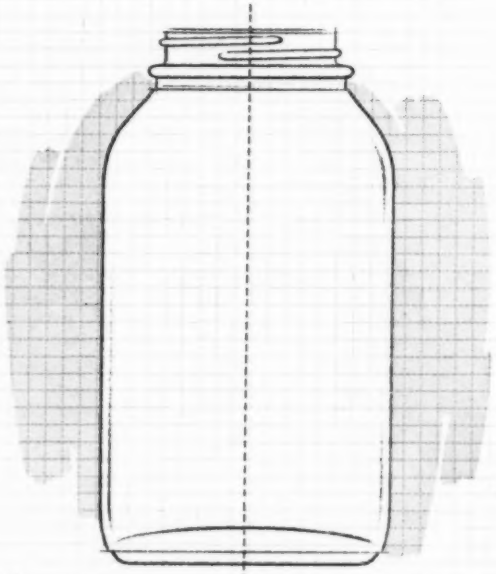
Who makes a package a SALESpackage?



A package designer who creates beauty to capture shopper's attention?



A package engineer whose concern is protection for the product inside?



A package merchandising expert who finds out what conveniences consumers want?

All three— design, engineering and marketing— may be necessary to solve your problems

Beauty of design will not be enough if you fail to meet requirements of high-speed filling lines. Product protection to the retail shelf may fall short of protection during actual use. The Owens-Illinois method of systematic investigation of packaging problems by engineers, designers and marketing experts is the big reason why successful packages so consistently come from Owens-Illinois.

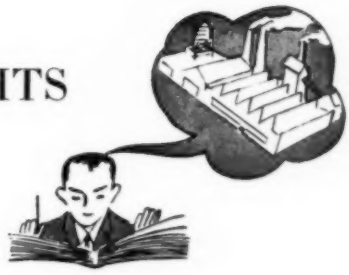
DURAGLAS CONTAINERS
AN (O) PRODUCT

OWENS-ILLINOIS
GENERAL OFFICES · TOLEDO 1, OHIO

Patent THOUGHTS AND TRENDS

*by Thomas Cifelli, Jr.**

PATENT ATTORNEY



Introduction

The following items are pin-pointed this month:

A patent battle is apparently brewing on *tetracycline* among some big antibiotic producers.

Chicago Federal Judge invalidates Arden-owned patent covering *aluminum chlorohydrate astringent.*

Patent Office Appeals Board turns down view that *uplifting the nose* by cosmetic means is not worthy of patent protection.

Among recent interesting patents is one for *treating air with gels* in place of wicks and another dealing with a *permanent wave lotion.*

Tetracycline Patent Situation

At the moment of writing, it is admitted that nothing authoritative is really known on what the press says is going to be quite a patent battle on tetracycline. Judging from press reports it looks as if the battle is going to be fought in the Patent Office and also in the courts. It seems that the Patent Office battle will be waged on the question of who gets protection on this antibiotic, American Cyanamid and Chas. Pfizer claiming priority.

Apparently, the press reports referred to indicate that there is an Interference in the Patent Office, and since such a proedure is not open to the public, the only way outsiders have of knowing what is going on is to follow the public press and use a lot of salt in evaluating the situation, as the press reports might not be accurate.

In addition to the Patent Office battle, the press also reports that American Cyanamid has filed a patent infringement suit against Bristol-Myers, claiming infringement of the Cyanamid patent covering Chlortetracycline (Aureomycin). Bristol is reported to be marketing tetracycline under its tradename of Polycycline to the Squibb Division of Olin-Mathieson and Upjohn. The Aureomycin patent was issued to Duggar on September 13, 1949 as No. 2,482,055.

It is hoped that some authoritative information will be available by next month, and if this proves to be correct we shall naturally pass it along.

*Newark, New Jersey

Stopette Not Stopped

The cosmetic trade has been wondering for almost five years what the courts were going to do with the Andersen patent, U. S. 2492085, dealing with the use of basic aluminum chloride in antiperspirants. It now knows the answer: The patent has been held invalid.

Litigation under the patent began in New York where the Reheis Company brought suit to have the patent declared invalid. That suit has been marking time in favor of a Chicago suit brought by Elizabeth Graham, who does business under the name of "Elizabeth Arden," against Jules Montenier. Reheis actually defended the Chicago suit for Montenier. It is understood that the parties agreed that whatever the decision was in the Chicago case it would be binding also in the New York suit. Consequently, the impact of the Chicago decision reaches New York also by reason of this agreement. While an appeal is understood to be a virtual certainty the situation as it now stands is that the Andersen patent has strikes against it in the two largest metropolitan areas of the U. S. A.

Patent Disclosure and Coverage

Andersen disclosed in his patent that astringent compositions containing aluminum chlorohydrate were desirable since they had the property of retarding perspiration, have no harmful effect upon fabrics, have no irritating effect upon the skin, and retain their effectiveness for considerable periods of time.

The patent asserts that aluminum chlorohydrate is markedly superior to aluminum chloride and aluminum sulfate, the conventional antiperspirants. In this connection, a one per cent solution of aluminum chlorohydrate is said to have as great an astringent action as a 15 per cent solution of aluminum sulfate. The patent attributes the desirable astringent properties of the chlorohydrate composition to the fact that the pH value is 4.38, which is considerably less acid than the corresponding solutions of aluminum chloride and aluminum sulfate.

Facts of the Case

Reheis sold to Montenier a product known as Chlorohydrol, the active ingredient in "Stopette." Montenier, as is well known, manufactures a line of cosmetics in Chicago, including the antiperspirant known as "Stopette."

Defense Against Patent

The defense was based on the contention that the Andersen patent did not involve invention because all that Andersen did was to substitute one form of basic aluminum chloride for another form of basic aluminum chloride that had been used in the prior art and that he did this just as soon as the new form was available to him. Also, the defense took the position that everything of substance contained in the Andersen patent was, in fact, worked out by Schofield Donald Company (which is the former name of Reheis) and that the essential idea was communicated to Andersen before he did any work with the basic aluminum chloride involved in the suit.

Issues in the Case

The judge framed the issues as follows:

(1) Is the basic aluminum chloride sold by Reheis Company, Inc. the same

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SPRINKLER TOPS
APPLICATOR PIPES

•

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as that described in the Andersen patent?

(2) Who first found that aluminum chlorohydrate is an effective anti-perspirant?

(3) Is the use of aluminum chlorohydrate as an anti-perspirant an invention in view of the prior art. Tied in with this problem is the question of whether or not the combination of aluminum chlorohydrate with an emulsifier is an invention.

Is the Basic Aluminum Chloride Sold by Reheis the Same as That Described in the Andersen Patent?

In reaching his answer to this question, the judge first asked how a new chemical material was to be characterized for patent purposes. He held that either of two methods is acceptable:

(a) A complete and correct molecular formula or

(b) A detailed description of how the substance can be made.

The judge held that while Andersen tried to use both methods, he was incorrect in his description by either approach and that there was no doubt in the judge's mind that the material described in Andersen's patent is not the material he actually used, and furthermore that the material supplied by Reheis is not the material that is described in the patent.

In arriving at his holding on these two questions, the judge made the following statement:

> (a) Aluminum chlorohydrate is described to a first approximation by Reheis and by Andersen as a basic aluminum chloride with a ratio of 2:1 for Al:Cl. However, the evidence of both the plaintiff and defendant discloses that the statement does not define the material because there can be no numerous substances with very different properties having this ratio of Al:Cl. It is necessary, therefore, to find a more detailed formula. The patent states that the probable formula of aluminum chlorohydrate is $Al_6(OH)_{18}CL_3$. The evidence is not consistent with the formula set forth in the patent. The plaintiff's witness Snell.....described conductivity measurements from which he concluded that the actual formula must be eight times that of the simple formula, i.e., $(Al_2(OH)_5Cl)_8$. If this conclusion is warranted, the molecular formula becomes substantially different from that given in the patent. The methods of estimating molecular size described by Neville..... seem more convincing than those of Snell. Neville concludes that the molecular size is more nearly 60 times that of the simple formula. In any event, the difference between Snell and Neville is only one of degree. The testimony of both expert witnesses proves that the formula given in the Andersen patent is incorrect.
>
> (b) When a complete molecular formula cannot be stated, the Patent Office seems to accept a clear description of how the material is made. Andersen specified in his patent that the aluminum chlorohydrate which he used was made according to the Huehn patent U. S. 2,392,531, that is, by the electrolysis of aluminum salt solutions. However, the evidence discloses that the aluminum chlorohydrate purchased from Reheis was made by the totally different method of reacting aluminum metal with an aluminum salt, Huehn patent U. S. 2,196,016 . . .; and it is clear from the evidence that Reheis never made chlorohydrol by the electrolysis method. . . . This evidence is corroborated by Defendant's Exhibit 8, a license from the Alien Property Custodian to use Huehn Patent U. S. 2,196,016 rather than the later electrolytic patent.
>
> The plaintiff takes the position that a soluble basic aluminum chloride made by either of these patents is essentially the same, but there is no evidence in the record to support this view. Merely because the ratio of Al:Cl can be made 2:1 in each case does not indicate that the materials would behave identically. If this argument were sound, it would also be necessary to accept the contention that a basic aluminum chloride made by still a third method, for example, that described in the testimony of Beekman . . . or one of those in Mellor. Treatise on Inorganic Chemistry, Volume 5, pages 277-278 (1924), . . ., also has essentially the same properties. In this event, there would have been no basis for the issuance of the patent, since a presumably equivalent basic aluminum chloride was known many years before the patent application.

Who First Found that Aluminum Chlorohydrate Is an Effective Antiperspirant?

Before attempting to answer this question, Judge Hoffman stated it was necessary to determine at what point a composition of matter becomes an effective antiperspirant. The judge adopted Snell's suggestion that an effective antiperspirant must meet the following requirements:

(a) It does not harm fabrics.

(b) It does not irritate the skin of a living human being.

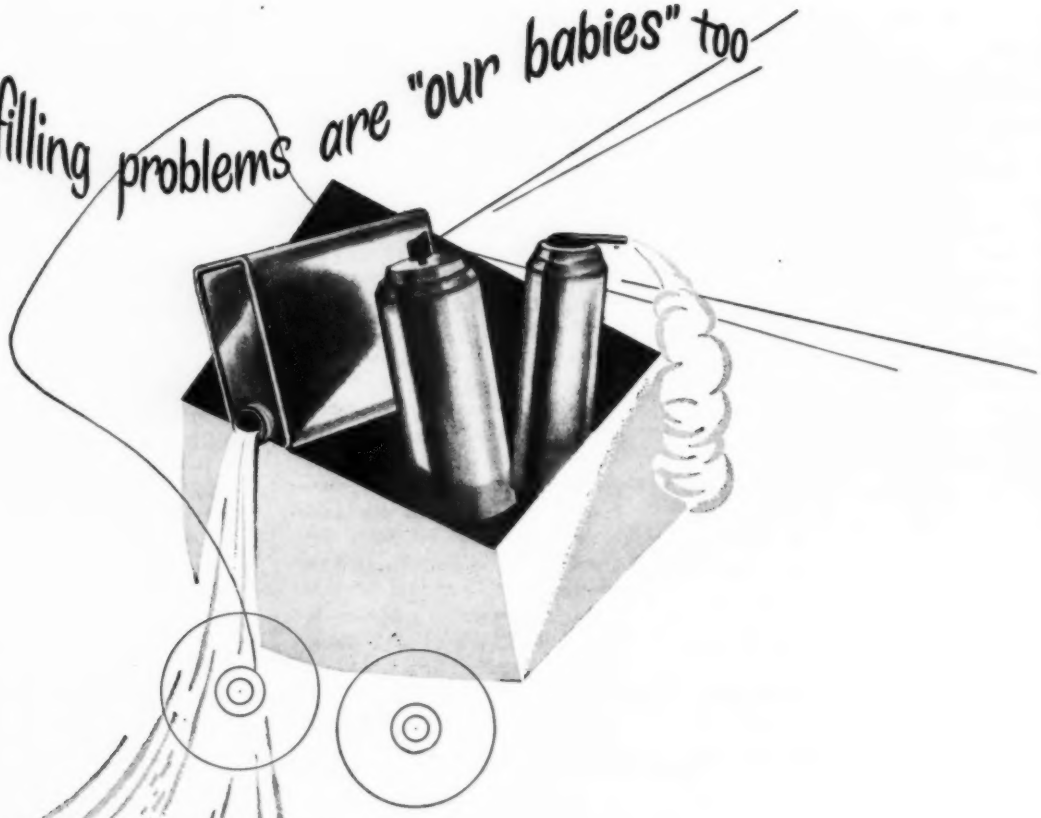
(c) It actually stops or decreases markedly the perspiration of a human being.

In considering whether these requirements were met by both parties, the judge made the following comments, which are believed to be of general interest far beyond the narrow issues of the case for they show not only how important it is to have experimental *data* but that it is necessary to have data which is pertinent and to the point:

> Tests of the first two requirements can be carried out by scientific procedures. Fabric deterioration tests have been standardized. Irritancy questions can be solved by accepted skin patch tests. Both of these tests were initiated by Reheis without any suggestion or contribution from Andersen. . . . The record demonstrates that the first test . . . was completed at least one year before Andersen even knew of chlorhydrol. In any event, Andersen concedes . . . that he obtained the data on fabric deterioration used in his patent from Reheis.
>
> We are warranted in concluding from this concession by Andersen that he also concedes that the idea that aluminum chlorohydrate could be an antiperspirant occurred first to Reheis, and that Reheis was the first to carry out the necessary experiments with some form of aluminum chlorohydrate, albeit perhaps not with a cream. The evidence is clear that the idea occurred to Reheis (or someone in his organization) long before Andersen even heard of the material. The defendant's Exhibit 15, especially the letter of April 18, 1946, is a complete disclosure of the essential information on aluminum chlorohydrate as a potential antiperspirant. A similar letter was admittedly read by Andersen before he started his work. . . . The Defendant's

(*Continued on page 692*)

Your filling problems are "our babies" too



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You'll like Continental's methods. Beginning with exhaustive chemical analysis of your product formula, we carry on with fast, efficient production accompanied by rigid quality control. Finally, we always stress our Midwest locations and shipping "follow-through." Continental's extensive warehouse space enables you to use our two plants as national distribution points. We handle shipping and paper work. Your orders are ready when you want them. And the savings on freight and reduced average damage are considerable, especially if you package in glass. Since Continental specializes in all types of filling . . . liquid, pressurized, and aerosol in glass or cans . . . combination shipments are routine. You get one bill of lading, one invoice, etc. Accounting is simplified. Shipments don't get snarled up. Dealers get their goods on time. All this . . . and more besides . . . is yours from Continental. Send us y(our) problem today.

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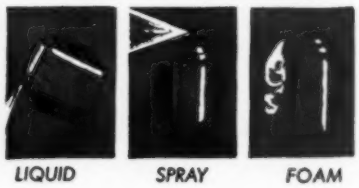

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DROPPING PARTS

Simplify Your Packaging Problem

#1

Non-rolling, extra-depth, Bakelite cap; thick-flange rubber bulb; Saftee-ball glass.

#3

Regular plastic cap; thin flange rubber bulb; semi-blunt glass.

#4

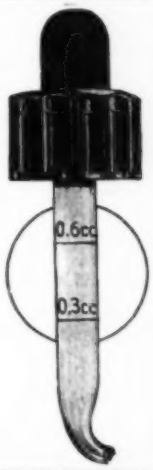
Metal cap; oil-resistant AMEKINE synthetic rubber bulb; blunt glass.

New Modernistic bottle. Designed to lie flat for convenient labeling. Oval front provides ample label space.

The wide variety of sizes, styles and colors in New Perfection's complete line of dropping parts offers the answer to your packaging problem. Each component part is designed to present and administer your product in the most attractive, convenient manner. We supply dropping parts to fit your bottles or furnish the complete unit.

DROPPER GLASSES CAN BE CALIBRATED IN COLOR

An inexpensive extra that adds great convenience to the use of your preparation. The dosage you desire in the color you specify is accurately and permanently printed on the dropper glass. Trade-marks and firm names can also be imprinted.



#2

Non-rolling, extra-depth Bakelite cap; thick-flange rubber bulb; special bent glass, plain or CALIBRATED.

RUBBER BULBS are supplied in many styles and colors. Oil-resisting AMEKINE synthetic rubber is used for oil preparations; natural rubber is supplied for other products.

CAPS of plastic or metal can be furnished in a complete range of sizes and colors.

DROPPER GLASSES are available in a wide variety of styles and sizes; plain or CALIBRATED in any color to mark specific dosages.

BOTTLES in an attractive modernistic style in Amber, Blue, Green or Clear glass are available, with dropping parts, in the following sizes: 2 cc, ⅛, ¼, ½, 1 and 2 oz.

Write for Samples and Quotations

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"Glass Goods of the Better Kind"

430 N. CRAIG ST. • PITTSBURGH (13), PA., U.S.A.

These flint glass bottles are from our C-39 line . . . one of our most versatile and attractive styles. Available in either clear glass or frosted and can be supplied plain or with your own fired-on ceramic label. Made in 14 sizes from 1/2 dram to 16 ounce capacity.

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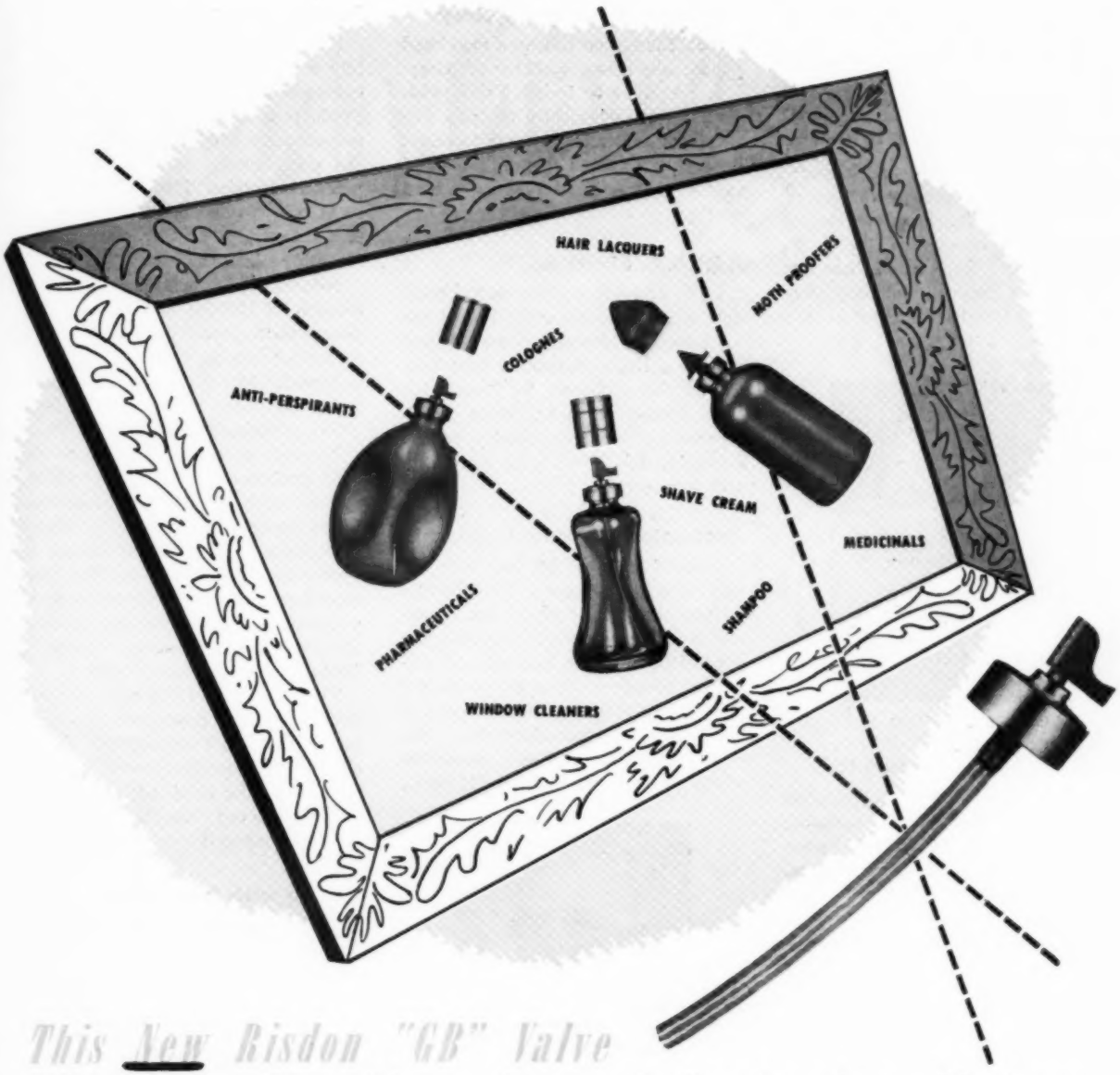

This New Risdon "GB" Valve Fits Into The Glass-Aerosol Packaging Picture

No Metal In Contact With Contents...
No Danger of Corrosion Of Valve Components

- In Performance and Appearance The "GB" Valve Is Tailored To Complement Bottle-Packed Spray Products.
- Applicable To Both Coated and Uncoated Bottles.
- Vertical Spray or Horizontal Spray.
- Protective Caps in metal or plastic available in custom-made designs to complement the product package.

Contact Risdon for further details on either the Model "GB" or Model JBR Valve.

RISDON

THE RISDON MANUFACTURING COMPANY • Valve Division
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RISDON'S JBR VALVE—KEY TO NEW AEROSOL POSSIBILITIES—NEW QUALITY PERFORMANCE AND STYLING FOR BOTH METAL AND GLASS CONTAINERS.

Makes possible the use of wider range of propellents. Uses all standard types plus "Freon-21", "Freon-22" and methylene chloride.

Sleek all-metal surface and cap enhance packages with a "quality look."

Produces a soft spray cloud of uniformly minute particles. Modified models can be supplied to give larger particle size, when required. Positive cut off.

Write for free descriptive folder.

RI-34

NEWS...

Lipscomb Heads J. B. Williams

Charles T. Lipscomb, Jr., formerly president of the Pepsodent division of Lever Brothers Co., has been elected president and director of the J. B. Williams Co. He succeeds the late Charles S. Campbell and will have offices in the Graybar Building in New York City.

CHARLES T. LIPSCOMB, JR.

N. Y. Office for Kinetic Div.

E. I. du Pont de Nemours & Co. has established a New York office to handle sales of "Freon" fluorinated hydrocarbon refrigerants, aerosol propellants, and miscellaneous products. It will be located in, and will function under, the New York district office of du Pont's organic chemicals department (40 Worth St.) which is headed by S. M. Conn.

Warren L. Hotmer, for the last three years New York area sales representative for the wholesale refrigerants section of the company's "Kinetic" Chemicals division, will be sales supervisor in charge of the newly established New York office.

Francis E. Cooper will be transferred from Cleveland to the New York territory as sales representative. Conde B. Keogh, formerly assigned to the Albany area, and M. J. Coppola, will assist Mr. Hotmer in the New York office.

William H. Brown, Jr., formerly sales representative in the Seattle territory, will take over Mr. Cooper's Cleveland territory, while Donald W. Nesbit, Jr., will move from Richmond, Va., to the Seattle territory.

M. Brooks Jackson, sales trainee in the Wilmington office, has been named sales representative in the Roanoke, Va., area.

Promoted by Dorothy Gray

Dick Livingston has been appointed general sales manager of Dorothy Gray, Ltd., according to Joseph Keho, president. He had been, for the past five years, assistant sales manager to James Boohecker who was recently advanced to the newly-created post of general manager.

A.M.A.A. Elections

L. W. Frohlich has been elected president of the Association of Medical Advertising Agencies and Robert Wilson and Mrs. Helen Haberman have been elected vice-presidents. Ira Nichols has been named treasurer, while Frank Dierson has been re-appointed general counsel and A. Douglas Brewer, executive secretary.

Appointed by Amer. Cyanamid

Thomas Floyd-Jones has been appointed sales manager of the pharmaceutical department of the fine chemicals division of American Cyanamid Co. He will supervise the bulk sales of antibiotics, pharmaceuticals and medicinal chemicals to ethical pharmaceutical and veterinary drug manufacturers. Mr. Floyd-Jones was formerly associated with Lederle Laboratories for 12 years.

THOMAS FLOYD-JONES

Appointed by Walker Labs.

George B. Feddersen has been appointed eastern division manager of Walker Laboratories, Inc., and Fred B. Beutlich, mid-western division manager, according to MacKay D. Holmes, vice-president in charge of domestic sales.

Cleveland Drug & Chem. Club

The Cleveland Drug & Chemical Club held its first Fall meeting on October 22 at the Hotel Carter. The Honorable Congresswoman Frances P. Bolton gave an interesting talk on the United Nations.

Heyden Buys Nuodex Stock

Heyden Chemical Corp. has entered into a contract to acquire all of the outstanding common stock of Nuodex Products Co., Inc., Elizabeth, N. J., manufacturer of chemical additives for the paint, plastic and other chemical process industries. The joint announcement was made recently by Simon Askin, president of Heyden, and Leo Roon, Nuodex president.

Nuodex will be operated as a separate division of Heyden under its present management, headed by Arthur Munich as general manager and executive vice-president. Mr. Roon, having reached retirement age, will withdraw from active participation in business.

Nuodex's domestic sales volume for 1953 amounted to about $6.5 million, and the volume of foreign business done by its wholly owned subsidiary, Nuodex International, in 1953, amounted to approximately $3.6 million. The company does business throughout the world with nine foreign affiliates and licensees and 45 foreign sales agents. Sales for 1954 are running ahead of 1953.

The acquisition of Nuodex is a logical step in Heyden's program of expansion as a manufacturer and supplier of both chemical intermediates and specialty products to the paint, protective coatings, plastics and other chemical process industries, according to Mr. Askin.

Young with Synarome

Benjamin Stanley Young has joined American Aromatics, Inc., and Synarome Corp. of America, according to Rene H. Bourguet, president.

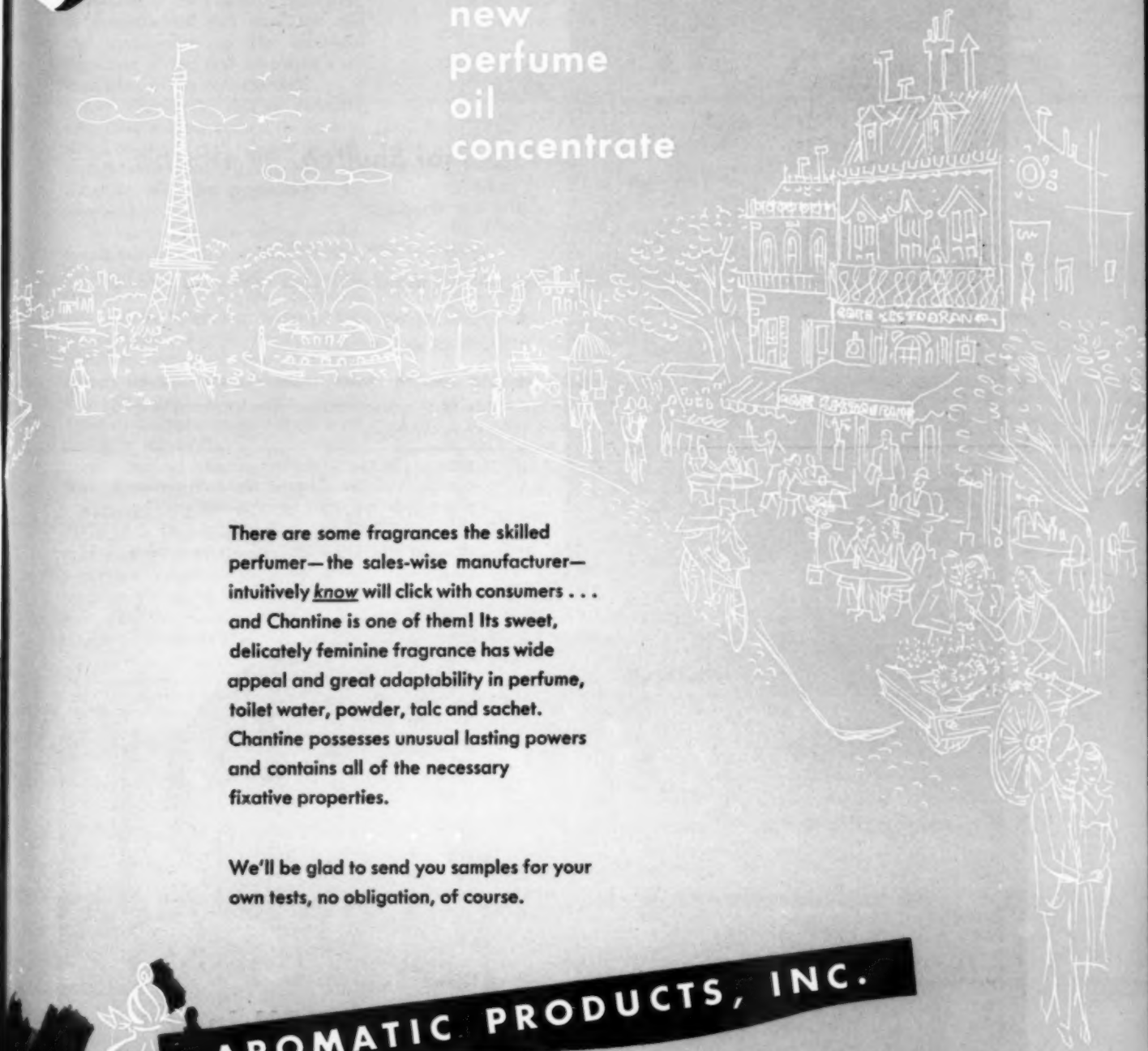
Shilts Named Treasurer

Allan R. Shilts has been elected treasurer of the Crown Cork & Seal Co., according to John J. Nagle, chairman of the board and president. He had formerly been on the controller's staff of the Ford Motor Co.

ALLAN R. SHILTS

Chantine

an exciting
new
perfume
oil
concentrate



There are some fragrances the skilled perfumer—the sales-wise manufacturer—intuitively *know* will click with consumers . . . and Chantine is one of them! Its sweet, delicately feminine fragrance has wide appeal and great adaptability in perfume, toilet water, powder, talc and sachet. Chantine possesses unusual lasting powers and contains all of the necessary fixative properties.

We'll be glad to send you samples for your own tests, no obligation, of course.

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Rhodinol Shulton, *for example . . .*

- a true Rhodinol
- made by a new process
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- approximately half the cost to you of similar material ex Geranium Oil
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Rhodinol Shulton is another successful product resulting from our extensive chemical research program. Among others now available are:

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Cosmetic Career Women

The newly formed Cosmetic Career Women held their first luncheon-meeting at the Waldorf-Astoria Hotel on September 28, with almost 100 members and guests present.

S. L. Mayham, executive vice-president of the Toilet Goods Association, as guest speaker, discussed some of the industry problems in which he believed the women should interest themselves. Introduced by Kay Colton, a member of the executive committee, he congratulated that committee and the membership on the successful launching of the first all-women's organization in the cosmetic field.

Kay Fitzpatrick, also an executive committee member, opened the meeting with a discussion of the aims of the Cosmetic Career Women, its organizational structure and the requirements for membership.

The executive committee has the following members: Clarice Mills Garland, Colgate Palmolive Co. and Peg Burrow, Oxzyn Co., representing manufacturers; Kay Colton, Morningstar-Nicol, Inc. and Annabelle Farrell, Emery Industries, Inc. (suppliers); Miriam Gibson French, *McCall's* (beauty press); and Kay Fitzpatrick, the Toilet Goods Association (representing a trade association in the field).

Nat. Aniline Branch in L.A.

National Aniline division, Allied Chemical & Dye Corp., has opened a branch office in Los Angeles which has a complete warehouse stock. It is located in Vernon at 4814 Loma Vista Ave. The telephone number of the branch is LOgan 8-2257.

DR. ALFRED E. EARL

DR. JURG A. SCHNEIDER

Hines, Pres. of Brayten

R. K. Hines has been elected president of Brayten Pharmaceutical Co., according to Lupton Patten, chairman of the board. Having formerly been an officer and director of Vick Chemical Co., Mr. Hines joined Brayten in 1951 as executive vice-president.

He succeeds Dr. John W. Bradley, prominent local physician, who sold his interest in Brayten and resigned his official duties in order to devote more time to science and medicine.

Ciba Promotions

Dr. Jurg A. Schneider, formerly senior physiologist of Ciba Pharmaceutical Products, Inc., has been promoted to director of physiology, and Dr. Alfred E. Earl, formerly senior research veterinarian has become director of veterinary research, according to Dr. Fredrick F. Yonkman, vice-president in charge of research.

D&O Achievement Award

Dodge & Olcott, Inc. has established a special "Achievement Award" to promote research and contribute toward product improvement and development in the meat packing industry. Hatton B. Rogers, D&O dry solubles division, announced the establishment of the new award during the program of the American Meat Institute Convention which was held from October 8 to 12 in the Palmer House, Chicago.

The award, to be presented annually, consists of $1,000 and a gold medal. It will be granted, "Without regard to age, sex or nationality, to the person who, in the opinion of the judges, has been responsible during the award year for the most outstanding achievement contributing to the growth and general welfare of the meat packing industry as a whole—whether in the fields of scientific research, operating or engineering."

The first award year will run from October, 1954, to June 1, 1955, when the nominations for the year will be closed. Presentation of the award will be made each year during the Annual Convention of the American Meat Institute.

First luncheon-meeting of newly formed Cosmetic Career Women at Waldorf-Astoria Hotel, September 28. Left to right, on Dais: Miriam Gibson French, *McCall's* Magazine; Kay Fitzpatrick, T.G.A.; Kay Colton, Morningstar-Nicol, Inc.; S. L. Mayham, executive vice-president, T.G.A., guest speaker; Peg Burrow, Oxzyn Co.; Clarice Mills Garland, Colgate-Palmolive Co.; and Annabelle Farrell, Emery Industries, Inc.

Propylene glycol U.S.P., produced by Carbide since 1931, plays many important roles in the Drug, Cosmetic, and Perfume industries.

PROPYLENE GLYCOL IN:

Drugs . . . More versatile than most generally used solvents, propylene glycol dissolves many pharmaceutically active substances. Consider it as your choice when preparing tinctures, solutions, and elixirs.

Cosmetics . . . Try propylene glycol in your cosmetic creams, lotions, and shampoos. This hygroscopic, water-soluble liquid enhances the softening action upon the skin and prevents "rolling" or drying out of the creams while in use, or in storage. In lotions and shampoos, propylene glycol couples the oil, lanolin, and soap in water.

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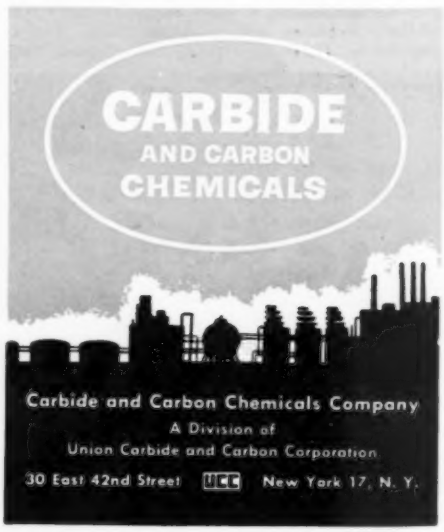
Whatever your use, propylene glycol from Carbide and Carbon will give top performance at your command. For further information write for your copy of the "Emulsions Booklet," (F-4186). Offices in principal cities. In Canada: Carbide Chemicals Sales Company, Division of Union Carbide Canada Limited, Toronto.



JOHN J. DENTON

THEODORE F. SCHOLZ

DR. RICHARD A. CAREY

Cyanamid Exec. Promotions

John J. Denton and Theodore F. Scholz have been appointed technical director and assistant technical director, respectively, of the Fine Chemicals division of American Cyanamid Co. They will supervise and be responsible for the product development work carried on in the laboratories of that division.

Dr. Richard A. Carey has been named medical technical director and will work closely with the research division of American Cyanamid on new product development, supervising clinical trials on products for the Fine Chemicals division. He will also act as medical advisor to the technical department.

Geigy Absorbs Alrose Div.

The sales and technical service staffs of the Alrose Chemical Company division have been absorbed by Geigy Industrial Chemicals, a new division of the Geigy Chemical Corp. This division has been organized to promote industrial sales of Alrose and Geigy products.

All inquiries and orders for Alrose products should now be sent to Geigy Industrial Chemicals, 89 Barclay St., New York 8.

Loynd Honored by Colorado

Harry J. Loynd, president of Parke, Davis & Co., was guest of honor at a banquet on October 7 given in the Colorado State Hospital, Pueblo, Colo. Governor Dan Thornton and others prominent in government, medical and pharmaceutical circles, were among approximately 300 persons at the affair sponsored by the Pueblo Lions' Club.

Mr. Loynd grew up in Colorado where he attended public schools and worked a regular shift in a drug store outside school hours. He graduated from the University of Utah in 1922 and, after several years in retail drug stores, joined Parke-Davis in 1931.

Package Machinery Appoints

Package Machinery Co. has opened a new office in Minneapolis which is headed by William Rangnow. Henry Nussbaum, formerly with the Marathon Corp., has been assigned to the Cleveland office. Joseph Bradford, formerly with the J. L. Ferbuson Co., has joined the Boston office. Richard Whittier, formerly with the Gates Rubber Co., is now on the sales staff of the home office. Ben Berk, a bakery specialist, formerly employed by the Lynch Corp., and Jack Egan, who was a salesman for the Ditto Corp., are now employed in the Chicago office. Hugh Holcombe has joined the Atlanta office.

Ernest A. Hhelm has been promoted to New York sales manager, while Robert S. Lyons of the Cleveland office, has been transferred to New York. John Kelley, formerly in the Springfield office, is now on the Philadelphia staff which is headed by Thomas L. Jefferson, Mid-Atlantic manager.

CSC Nitroparaffin Plant

Commercial Solvents Corp. has begun construction of a $5 million large-scale Nitroparaffin plant at Sterlington, La. It is expected to begin operation in August, 1955.

The company is presently producing and marketing limited quantities of Nitroparaffins and derivatives, which have already achieved a wide range of applications in chemical and chemical process industries.

In addition to the new construction at Sterlington, the company's existing Nitroparaffin derivatives facilities at Peoria, Ill., will be enlarged.

Upjohn Transfers Reames

Dr. Harold R. Reames has been transferred from the medical division of the Upjohn Company to the research division as head of the department of infectious disease, according to Dr. E. G. Upjohn, president.

Harry J. Loynd, right, president of Parke, Davis & Co., receiving a certificate of appreciation from Colorado Governor Dan Thornton for his "service to humanity." Looking on is Dr. F. H. Zimmerman, center, superintendent of the Colorado State Hospital. Award was made at banquet on October 7 in honor of Mr. Loynd.

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BASSES - ALPES, FRANCE

Bringing the harvest to the distillery

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Give Talks on Fragrance

Kay Jamesson gave a talk on "How to Merchandise and Promote Fragrance Products" to about 100 toilet goods buyers and store managers of the Belk Buying Stores during that organization's annual sales meeting in Charlotte, N. C., on October 5.

Frazer V. Sinclair, *Beauty Fashion*, also a guest speaker, talked on how "The Whole World Contributes to the Making of Perfume." Two 15-minute color films were shown, in conjunction with Mr. Sinclair's talk, depicting the sources of the ingredients that go into the making of perfume.

The half-day program was devoted entirely to discussions on the promotion of fragrance products.

Left to right: Kay Jamesson, executive director of Fragrance Foundation; Dr. Robert Prindle, Lehn & Fink; Jan Castleberry, beauty consultant, Revlon Products; Eli Davidson, North Carolina sales representative for Revlon; Bernice Magruder, salesrepresentative, Helena Rubinstein; and Frazer V. Sinclair, Beauty Fashion, attending annual sales meeting of Belk Buying Stores, held in Charlotte, N. C., October 5. Talks were given by Mrs. Jamesson, on fragrance, and by Mr. Sinclair, on the making of perfume.

Package Mach. Celebration

The Package Machinery Co. held a First Anniversary celebration of its Philadelphia office at the Black Horse Tavern on September 30, with many customers and representatives of various business publications present.

Roger L. Putnam, chairman of the board and director of sales, and J. J. Kelly, field sales manager, were on hand to greet the visitors. Thomas L. Jefferson, Mid-Atlantic manager, who was on temporary duty as Lieutenant Commander in the Navy, received special leave to attend the celebration.

Thompson with Rhodia

Warren B. Thompson, formerly with E. I. du Pont de Nemours & Co., has become associated with Rhodia, Inc., as sales representative in the Middle Atlantic states, with headquarters in Philadelphia.

He will be responsible for sales of aromatic chemicals to the perfume, toiletries and soap industries and for the sales of the products of Rhodia's industrial reodorant division.

WARREN B. THOMPSON

Stocking Rejoins Upjohn Staff

Dr. Gordon G. Stocking has rejoined the department of veterinary medicine of the Upjohn Co., according to Dr. E. L. Burbidge, medical director. He will be concerned principally with the development and use of products in large animal medicine.

He had formerly been the resident veterinarian at the Upjohn Richland Farms from 1946 to 1949 when he joined the veterinary staff of the Upjohn Co. In 1951 he left the company to assume the managerial responsibilities of the Arabian horse program at the Kellogg Ranch Unit, California State Polytechnic College, at Pomona. He subsequently served for two years as the battalion veterinarian for the 4th Field Artillery, U. S. Army, before returning to Upjohn.

Appointed by Ivers-Lee

James P. Measday has been appointed sales manager for the Ivers-Lee contract packaging division of Ivers-Lee Co. He had formerly been assistant sales manager.

JAMES P. MEASDAY

Winthrop Receives Award

Winthrop-Stearns Inc. recently received a special award from President Eisenhower's Commission on Employment of the Physically Handicapped for its meritorious record in employing physically handicapped workers.

A certificate of award was presented by the President's Commission, which is affiliated with the U. S. Department of Labor, to Donald S. Shepherd, divisional vice-president of Winthrop's manufacturing plant in Myerstown.

Of the firm's total working force, 12 per cent are handicapped in some form. In order to qualify for the award, a concern must employ a minimum of five per cent handicapped workers.

In accepting the certificate, Mr. Shepherd noted that Winthrop's policy of hiring the handicapped has been in effect since the plant began operations in Myerstown in 1948. This policy was set by the firm's president, Dr. Theodore G. Klumpp, formerly chairman of the Office of Defense Mobilization's Task Force on Employment of the Handicapped.

Sales Mgr., Smith-Dorsey

Dwight Duke has been appointed sales manager of the Smith-Dorsey division of the Wander Co., according to V. T. Johnson, vice-president. He was formerly assistant sales manager.

Atlanta Drug Golf Tourney

The Atlanta Drug & Chemical Club held its first annual golf tournament at East Lake Country Club on September 17. Maurice Hoops, regional manager, Merck & Co., won low net and is the first to have his name inscribed on the trophy. The tournament was followed by a dinner at the club.

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(Brand of Hexachlorophene)

The market for products containing G-11 is an established, growing market with virtually unlimited opportunities for profitable development.

Few products have ever been studied so exhaustively and given such unanimous acclaim by authorities. G-11 is recognized as the proven, effective and non-irritating antiseptic chemical that offers outstanding hygienic and deodorizing advantages.

Years of safe, successful use by millions of people assure the continued success of your products containing G-11.

As the originator and producer of G-11, Sindar offers you the benefits of its scientific knowledge, practical marketing experience and technical service in using it to the best advantage in your soaps, detergents and cosmetics.

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DR. EMIL G. KLARMANN

Klarmann Named Lecturer

Dr. Emil G. Klarmann, vice-president and manager of technical services of Lehn & Fink, Inc., and first vice-president of the Chemical Specialties Manufacturers Association, has been appointed Lecturer in the Department of Dermatology and Syphilology of the New York University Post-Graduate School of Medicine.

Kimble Award, Nobel Prize to Research Team

The 1954 Kimble Methodology Research Award, sponsored by the Kimble Glass Co., was presented to a three-man research team last month which discovered a simple method of growing polio viruses in quantity in test tubes. Recipients of the annual award were Dr. John F. Enders, director of the research division of infectious diseases at Children's Medical Center, Boston, and Associate professor of Bacteriology and Immunology at Harvard University's Medical School; Dr. Thomas H. Weller, assistant director of the research division of infectious diseases at Children's Medical Center; and Dr. Frederick C. Robbins, director of the department of pediatrics and contagious diseases at City Hospital, Cleveland, and professor of pediatrics at Western Reserve University School of Medicine.

The Kimble Award includes $500 in cash and an engraved plaque.

These three men, on October 21, received international acclaim for their work in polio research when they were awarded the Nobel Prize for medicine and physiology. They will share approximately $36,000 and will each receive the Nobel Medal, made of eight ounces of gold, and an illuminated diploma, on December 10. This date is the anniversary of the death (1896) of Alfred Nobel who set up a fund to provide annual cash prizes for achievements in the fields of medicine, physics, chemistry and literature, and for the Nobel Peace Prize.

MATTHEW A. PHELAN

Appointed by D&O

Hatton B. Rogers, formerly director of technical service for the Huron Milling Co., has been appointed director of the dry solubles division of Dodge & Olcott, Inc.

Matthew A. Phelan has joined the company's sales organization, and after several weeks' training in the Dodge & Olcott laboratories, will be transferred with the Philadelphia branch office.

Consulting Chemists Elections

Charles Davidoff, consulting chemical engineer, was elected president of the Association of Consulting Chemists and Chemical Engineers, Inc., last month at the annual meeting. Lincoln T. Work, also a consulting chemical engineer, was elected vice-president; Elliot A. Haller, president of Haller Testing Labs., became secretary; and Percy E. Landolt, Landolt & Whitney, was elected treasurer.

J. GORDON WILLS

Wills with Crown Cork

J. Gordon Wills has been appointed division manager of manufacturing by the Crown and Closure division, Crown Cork & Seal Co., according to Fred J. Wood, vice-president of the company and general manager of the division.

Ellegood Appointed by S&D

Dr. John A. Ellegood, director of pharmaceutical control for Sharp & Dohme since 1946, has been appointed to succeed Dr. Paul S. Pittenger as director of quality control.

D'Aigremont Returns

Jacques d'Aigremont, executive vice-president of Roure-Dupont, Inc., recently returned from a three-month business and pleasure trip through Europe, having covered areas responsible for the supply of many of the firm's important raw materials.

Dr. Thomas H. Weller, center, member of three-man research team which discovered method of growing polio viruses in test tubes, accepting Kimble Methodology Research Award from Dr. H. Gilbert Crecelius, right, president of Conference of State and Provincial Public Health Laboratory Directors. E. J. Rhein, left, of Kimble Glass Co., sponsor of award, looks on. Dr. Weller, along with Dr. John F. Enders, directors of Research Division of Infectious Diseases at Children's Hospital, Boston, and Dr. Frederick C. Robbins, director of Department of Pediatrics and Contagious Diseases, City Hospital, Cleveland, received international recognition later in month as research team by being awarded Nobel Prize.

MAX A. MINNIG

Minnig, V.P., Witco Chemical

Max A. Minnig has been elected executive vice-president of Witco Chemical Co. He was formerly vice-president of the firm.

DAVID J. WARNER

Warner Joins Fleuroma

David J. Warner, sales manager for a private brand soap manufacturer for the past 14 years, has joined the sales force of Fleuroma, Inc. Mr. Warner has served in several capacities for the Cosmetic Industry Buyers & Suppliers Association (CIBS) and, at present, is first vice-president.

New Research Lab. for Baker

J. T. Baker Chemical Co. is planning construction of a new research laboratory building adjacent to the main plant in Phillipsburg. The three-storey structure will provide about 20,000 square feet of floor space. A windowed, two-storey section on the left will contain the various laboratories for both inorganic and organic chemical investigations and for X-ray, spectroscopic and other physico-chemical studies. A three-storey section on the right will provide for the offices of the Baker Research division, the Baker Research Library and the offices of the *Chemist-Analyst* and Baker Information Services.

Cos. Chemists Program

The Society of Cosmetic Chemists will hold its annual meeting and Medal Award Dinner on December 9 at the Hotel Biltmore, New York. Four papers will be delivered during the morning session: "The Use of Acylated Amino Acids in Cosmetics," by H. W. Zussman and W. Lennon, Geigy Industrial Chemicals; "The Physical Chemistry of Stearic Acid," by C. C. Tillotson, Procter & Gamble Co.; "Polymorphism of Glycerides Distinguishable by X-ray Diffraction," by E. S. Lutton, Procter & Gamble Co.; and "The Use and Newer Applications of the Silicone Compounds in Dermatology and Cosmetics," by I. I. Lubowe, Skin and Cancer Unit, N.Y.U.-Bellevue Medical Center, New York.

Four more papers will be delivered during the afternoon session: "Newer Aspects of Epidermal Differentiation," by Peter Flesch, University of Pennsylvania, Department of Dermatology; "Alterations in the Skin Physiology Following Continuous Use of Soaps and Detergents," by D. J. Birmingham, U. S. Public Health Service; "The Mechanism of Percutaneous Penetration and Absorption," by Stephen Rothman, University of Chicago, Dermatology Section, Department of Medicine, Chicago; and "The Physiology and Histo-Chemistry of Hair Growth," by H. B. Chase, Brown University, Providence, R. I.

Added to MMR Sales Staff

Howell Rile and William Bruce Wallace have joined Magnus, Mabee & Reynard, Inc., as sales representatives in the Metropolitan New York area, under the direction of M. Stanley Barker, assistant vice-president. Mr. Rile will represent the company in parts of Brooklyn and Long Island, and Mr. Wallace, in Manhattan, the Bronx and Westchester.

T. G. A. Progran

The Scientific Section of the Toilet Goods Association will hold its meeting in the Starlight Roof, Waldorf-Astoria Hotel, on December 8. The following papers will be delivered: "Practical Aspects of Suntan Formulations," by I. R. Hollenberg, technical director, Knapp Products, Inc.; "Acetylated Monoglycerides and Their Potential Use in Cosmetics," by Everett G. McDonough and Walter W. Edman, Evans Research & Development Corp.; "Dermal Sensitization," by Dr. Thomas W. Tusing, Hazleton Laboratories; "Inhibition of Dental Caries by Dentifrices—Laboratory Predications versus Clinical Results," by Dr. R. S. Manly, Tufts College Dental School; "Meterspray and Its Application in the Cosmetic and Pharmaceutical Fields," by H. R. Shepherd, vice-president in charge of research and development, Connecticut Chemical Research Corp.; Effect of Estradiol or Methyltestosterone on the Skin and Hair Growth of Rats," by Amos E. Light, Wellcome Research Laboratories; and "The Mercaptan-Disulfide System in Permanent Waving —A New Mechanism and Its Practical Implications," by Ross Whitman and Milton G. Eckstrom, Rayette, Inc.

R. D. Webb Named Treasurer

Richard D. Webb has been appointed treasurer of W. J. Bush & Co., succeeding his father, the late Richard Righton Webb. Mr. Webb, a great-grandson of the founder of W. J. Bush & Co., established in London, England, in 1851, was closely associated with his father in the conduct of the business during the past five years.

Bergman with Plume & Atwood

Lawrence Bergman has been appointed sales manager of cosmetic products by the Plume & Atwood Mfg. Co., succeeding Russell Johnson.

Architect's drawing of new research laboratory building, J. T. Baker Chemical Co., which will be located adjacent to Baker's main plant in Phillipsburg.

VERONOL

AN ALDEHYDE

Typical Specifications:

PHYSICAL APPEARANCE:	Light yellow liquid.
ODOR TYPE:	Aldehydic; suggestive of a mixture of higher aliphatic aldehydes.
SOLUBILITY:	10 parts soluble in 100 parts 80% Ethyl Alcohol.
STABILITY:	Stable in soaps, cosmetics and perfumes.
REFRACTIVE INDEX $n\frac{20}{D}$:	1.4525
SPECIFIC GRAVITY $\frac{20}{20}$:	0.8500
SUGGESTED USES:	As an ALDEHYDE TOP NOTE . . . 1/10 to 1/2%. *Extremely powerful*, it is an interesting addition to existing fragrances to add life and improve character of bouquet.
QUALITY:	Highly purified for use in fine perfumes. Held to rigorous specifications by our control laboratory.

Note these additional VERONA specialties

BERGAMOT SYNTHETIC P-1104 • RESEDALIA

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Sole representatives in the United States for: J. & E. SOZIO, GRASSE, FRANCE

RESINOIDES • NATURAL ABSOLUTES • ESSENTIAL OILS

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PRODUCTS BUILD SALES FOR *Your* PRODUCTS

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Hoya Carnosa is in a class by itself–

So are **DREYER** Synthetic Scents

The waxen flowers of *Hoya Carnosa* have something rare and fragrant.

Their perfume is memorable. It has its own distinction. Nature does not duplicate it.

You can't get it even from Dreyer . . . which is so adroit in re-creating even the subtlest natural flower odors.

And a Dreyer Floral Essence—besides having the unique characteristics of the natural flower perfume—seems to have greater power to last—with more uniformity, too.

So the quality you want is always kept high, and the costs you must watch are kept low. Send today on your letterhead for free samples.

FLAVORS
ESSENTIAL OILS
AROMATIC CHEMICALS

depend on *Dreyer* **for**

P. R. DREYER, Inc. 601 WEST 26th STREET, NEW YORK 1, N. Y.

Conart Moves to New Plant

The Conart Co. Inc., manufacturer of molded closures and other plastic items, formerly in Long Island City, has moved to a new plant at Glen Head Road, Glen Head, Long Island. Having expanded into the new factory, Conart has greatly increased its production capacity and installed numerous devices and machines to improve and control the quality of production. The company is also producing electrical parts and other plastic items using large-volume production methods.

McGraw with Onyx Oil

Ralph O. McGraw, Jr., formerly with the Kraft Chemical Co., has been appointed to the sales staff of Onyx Oil & Chemical Co. and will work out of the Chicago office.

RALPH O. McGRAW, JR.

Cos. Chemists Seek N. Y. Chapter

A meeting of Cosmetic Chemists was held on September 29 at the Brass Rail Restaurant, New York, for the purpose of organizing a local chapter of the Society of Cosmetic Chemists. Forty-seven members and friends of the parent organization were present. Officers were elected and committee chairmen appointed to proceed with the details of organization and also to petition the National Society for a charter.

The officers and committee chairman are Michael A. Stanton, chairman; William Lambert, vice - chairman; Warren Dennis, secretary; Theodore Ostrowski, treasurer; Dr. Louis C. Barail, publicity; Gabriel Barnett, program; Dr. Paul G. I. Lauffer, by-laws; and Miss Hazel Bishop, entertainment.

Crown Cork Buys Seal Stik

Crown Cork & Seal Co. has purchased Seal Stik, the plastic swivel stick formerly made by Beemak Plastics of Los Angeles. It will now be manufactured by Crown's specialty division in St. Louis.

New plant of the Conart Co., Glen Head, L. I., where firm recently moved. The facilities offer a greatly increased production capacity as well as many devices and machines for improving and controlling quality of production.

Armour Moves Gen'l Office

The general office of Armour Laboratories has been moved to Kankakee, Ill., having formerly occupied two floors at 520 North Michigan Ave., Chicago. All executive and administrative personnel and equipment are now in the new Armour Pharmaceutical Center at Kankakee, according to Edgar L. Patch, general manager of the Laboratories, who stated that only the Chicago district sales office, under Albert C. Gunsaulus, will remain at the old address.

New Branch for A. H. Robins

The A. H. Robins Co. has opened a new branch in Los Angeles at 6444 E. Fleet St. which contains 22,000 square feet of floor space. The modern, coordinated warehouse and office unit will enable the company to give quicker service to customers in 11 western states as well as in Alaska and Hawaii, according to C. B. Howell, western regional sales manager.

Beatrice Krone

Beatrice Krone, wife of Robert Krone, head of Fritzsche Brothers' flavor sales division, died last month following a prolonged illness. Both Mr. and Mrs. Krone participated actively for many years in the affairs of the Flavoring Extract Manufacturers Association, on whose convention committee Mr. Krone has served for the past two years.

Dr. Charles I. Post

Dr. Charles I. Post, vice-president of Nopco Chemical Co., in charge of its vitamin division, died October 10 at his home in Short Hills, N. J. He was 56 years old.

He joined the company in 1925. He had been sales manager of the Vitex Laboratories division of Nopco, general sales manager of the vitamin division and assistant sales manager in charge of vitamin sales before becoming vice-president.

Earl Beck

Earl Beck, executive vice-president of Eli Lilly & Co., died unexpectedly at his home, October 15, following a heart attack. He was 59 years old. He had been associated with the company since 1914 when he joined the firm as a motion-and-time-study trainee in what was then known as the efficiency division. Later, he advanced to director of that division and in 1944 was named vice-president of industrial relations.

Henry T. Stanton

Henry T. Stanton, 67, chairman of the board of the Rystan Co., and partner of the firm, died at the Palo Alto Hospital, Palo Alto, Calif, on October 7. He was also vice-president and western manager of the J. Walter Thompson Advertising Agency, residing in Woodside, Calif.

Surviving are his wife, Mrs. Louise Collier Stanton; three sons, Henry T. Stanton, Jr., James H., and Charles C.; and a daughter, Mrs. John Van Nortwick, Jr.

Charles P. Tyrrell

Charles P. Tyrrell, honorary secretary-treasurer of the Proprietary Association, died on October 16 at the Memorial Hospital, Bradenton, Florida. He joined the Association staff about 1907 and served the organization faithfully until he retired to his home in Bradenton in 1954.

He is survived by his wife.

Richard Righton Webb

Richard Righton Webb, president of W. J. Bush & Co., and grandson of the founder, died in the Park West Hospital on October 7 of a heart attack. He was 60 years old.

Born in London, Mr. Webb came to the United States in 1922 where he resided at Den Road, Stamford, Conn. He is survived by his wife, Mrs. Lydia Webb; a son, Richard D., and four sisters who live in England.

DOW

SHE BUYS THE *"Soothing Effect"* THAT ONLY PROPYLENE GLYCOL, U.S.P.. CAN GIVE

PROPYLENE GLYCOL, U.S.P., ***gives lotions and creams a soothing and softening effect without stickiness—makes new customer favorites out of old-line products***

Propylene glycol, U.S.P., by Dow, replaces a more expensive ingredient in many creams and lotions—and makes them better products, too. This means more economy in formulation for you, more sales appeal for your product.

Propylene glycol is a very effective carrier, emollient, humectant and preservative for many types of cosmetics—lotions, creams, cold creams and sun tan preparations. And it may be safely used with all types of lotions —nonalcoholic, mildly alcoholic and even strongly alcoholic.

Want to make it better, make it for less? Better check Dow propylene glycol, U.S.P., with its unique soothing effect. For your free sample and more complete information, write to THE DOW CHEMICAL COMPANY, Midland, Michigan, Dept. OC-831G-1.

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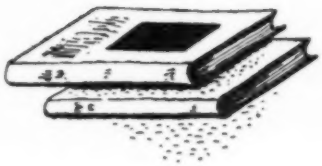


Trade Literature

"Alva" Pharm. Flavors

Pharmaceutical flavors under the Alva trademark of van Ameringen-Haebler, Inc., 521 West 57 Street, New York 19, are the subject of an interesting catalog recently issued by this firm.

Bulletin on Thymidine

Researchers in pernicious anemia and in studies on nutrition will be particularly interested in the new bulletin No. 141 on thymidine issued by Schwarz laboratories, 230 Washington Street, Mount Vernon, N. Y. The importance of this key metabolite is indicated by its presence in deoxyribonucleic acid, a component of the genes which control heredity and regulate growth in all living cells. Limited studies thus far made have also shown it to be of special significance in formation of red blood cells, particularly in reactions involving vitamin B_{12} and folic acid.

The bulletin gives the structural formula, physical, chemical and biochemical properties, briefly outlines its therapeutic effects shown by clinical trials, and contains a list of references.

Swift Booklet

Swift & Company, Industrial Oil Department, 1800 165 Street, Hammond, Ind., has issued an eight-page bulletin which catalogs all of the firm's industrial oil and fatty acid products. Included are detailed specifications, shipping information, and suggested usage on products of animals, vegetable, and marine origin including: oleic acids, red oils, stearic acids, glycerines, hydrogenated and sulfonated products; tallow, lard oils and stearines, as well as data on specialized products including defoamers, esters, metal and wool processing oils and spermaceti USP.

Daigger Apparatus Digest

Last month A. Daigger & Company, 159 West Kinzie Street, Chicago 10, published the first expanded issue of Daigger Apparatus Digest. This is a sixteen-page, illustrated booklet.

Croda Bulletin

Croda, Inc., 51 Madison Ave., New York, has issued a four-page bulletin on Croda glycerol mono-stearate and other glyceryl and glycol esters, giving the average analysis of 10 products, together with suggested uses. Croda has also issued a four-page bulletin on Cithrol polyglycol esters—a range of non-ionic surface-active agents.

Methyl Cellosolve Acetate

A new four-page technical information sheet on methyl cellosolve acetate has been issued by Carbide and Carbon Chemicals Company, 30 East 42 Street, New York 17.

Fischer & Porter Instruments

Fischer & Porter Co., Hatboro, Pa., has issued a general catalog with illustrations, descriptions, and basic specifications of the firm's complete line of process instruments. Instrumentation for measuring and controlling process variables includes: Variable-area and variable-head flow meters; pressure instruments; temperature instruments; liquid level instruments; density and specific gravity measuring instruments; viscosity and consistency instruments; electric, pneumatic, and electronic transmitting, recording and controlling instruments with alarms and integrators; and air-operated control valves.

Molybdenum Data Bulletins

Climax Molybdenum Company, 500 Fifth Ave., New York 36, has announced a new series of molybdenum data bulletins which are designed to provide, in concise form, authoritative data on the properties of molybdenum compounds. The first bulletin, entitled Properties of Molybdenum Oxide, is now available. Other titles to appear at intervals during the next year include, Thermodynamic Properties of Molybdenum Compounds, Molybdenum Pentachloride, Simple Molybdates, Complex Molybdates, and Organic Molybdenum Complexes.

The Low Cost of Medicines

Schering Corporation, Bloomfield, N. J., has issued a 76-page booklet entitled, The Low Cost of Medicines. This consists of the reprinting of a symposium by the leaders of the pharmaceutical industry and the medical profession which originally appeared in the August, 1954, issue of the American Professional Pharmacist. The purpose of the symposium is to correct the misconception held by the public that drugs and medicines are costly. Twenty-five different titles are listed in the symposium.

The man who knows his punches and dies says "Send for our Stokes booklets on 'What You Should Know about Punches and Dies' and 'How to Save Money on Punches and Dies' . . . and tell us how many you need."

"What Should You Know About Punches and Dies?"

"The answer is to get punches and dies which will make good tablets for the longest possible time.

"That was a problem to us over 50 years ago when we started to make tabletting machines. We soon found we had to make our own punches and dies.

"Now, after a half-century of experience we have a big department, skilled hands, all sorts of precision machines . . . just for making punches and dies.

"Lots of our experience is with *making* punches and dies; but a lot of it, too, is in *using* them in our own laboratory. So we've sorted out our knowledge and put what you should know in two booklets: 'What You Should Know About Punches and Dies' and 'How to Save Money on Punches and Dies'.

"They're the sort of booklets that are useful to everyone from the Purchasing Agent to the machine operator.

"Usually, when you buy a tabletting machine, you get an instruction book which gives plenty of good advice. But after several years, and many changes of operators, who knows what's become of the little instruction book?

"Our two booklets can be truly helpful. We've printed them in quantity, so if you need a batch, just say the word!"

F. J. Stokes Machine Company
Philadelphia 20, Pa.

STOKES

STOKES MAKES: High Vacuum Equipment, Vacuum Pumps and Gages / Industrial Tabletting, Powder Metal and Plastics Molding Presses / Pharmaceutical Equipment

Management Forum

by Francis Chilson
INDUSTRIAL CONSULTANT

A LETTER FROM ONE OF THE BOYS

"Dear Mr. Chilson

First I must beg you to excuse the script. However, for the sake of plant and office morale I feel it more politic not to air my opinions through a secretary. I can't type worth a damn and so I hope you will struggle through this.

To begin with I should like to congratulate you on your column in D. C. I. Of course I can't always agree with you, naturally those are the times when I feel you are slipping. But most of the time, I find you a valuable ally in slugging it out with the boys who sign the checks. Particularly I call down blessings on your head for your remarks on Comptrollers and more recently on Personnel theorists. God! do they (particularly the latter) give me a bellyache! and how much have your remarks been needed!

Nominally I'm only supposed to be running a laboratory here and take care of trouble in the production line when it raises its ugly head. In practice I seem to get rung in on everything from development to advertising and sales, and not infrequently on personnel problems, and it follows that comptroller and personnel theorists are being constantly combed out of my hair. I know all about, "It isn't the money, it's the principle etc.," when it comes to spending $20.00 of a clerk's time to trace down the usage of $3.50 worth of machine parts, but I still hold tightly to the theory that it bloody well *is* the money. As a friend of mine in a similar position remarked, "They've got more records on production than production has." Fortunately we've been able to keep it under control here, but I've been in plants of similar size where employees could have been filching 10% of production and it still would have been cheaper than maintaining the records they do.

About personnel, I will hold myself strongly in hand so as to keep this coherent. Maybe you can tell me, however, why in hell it doesn't occur to some of those people, that the best principle of human relations is to look on people as humans. We have a plant manager, bless him, he is a fine, competent executive and engineer. He is also a naturally kind and courteous person, but he will just insist on reading every book and attending every course available on personnel or human or employee relations. It's all I can do to convince him periodically, that fingerprints or Rorschacks or vaginal smears, for all employees are not really essential to modern production or human relations. It's true that he does send all employees a nice card on their birthdays but he still is not convinced that when a normally pleasant-natured man gets grumpy there's no urgent necessity for a psychoanalyst. It may be that the new baby is keeping him up at night. And there is another thing: Why shouldn't it be obvious even to a personnel man that a pleasant neighborly interest (not snooping scientific categorizing) in a man, ('How's with little Mary's teeth?' or 'Is the baby gaining better now?') is at least equal to, and often a hell of a lot better than, any routine good will such as birthday cards. Oh well, you know what I mean.

I hope you have been able to read this far. Even if you haven't its been nice to pour out my peeves into ears other than my wife's. Suffice to say that I enjoy, and profit from your column. Technical knowledge combined with common sense is a rare commodity. You are blessed, and it is good of you to share your blessing. Long may you write."

A PROPHECY

On March 8, 1941, the late Senator Arthur Vandenburg lost his fight against the Lend Lease Bill. He opposed it not because it was the only way at that time to aid Britain but because it would eventually "turn the White House into G. H. Q. for all the wars of the world." That night the beaten, disillusioned Senator wrote the following comment in his diary and how very right he was! . . .

"This is what I believe was the result: We have torn up 150 years of traditional American foreign policy. We have tossed Washington's Farewell Address into

RELIEF REACHES MILLIONS

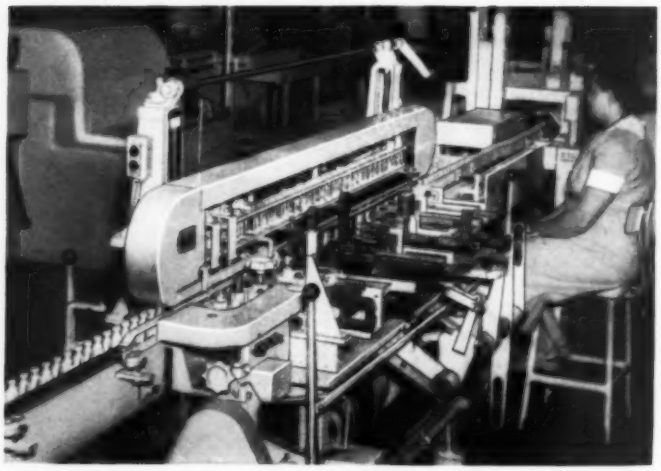
with the help of

PNEUMATIC

A familiar bottle in medicine chests, desk drawers, pockets and handbags, St. Joseph Aspirin is a highly respected and effective remedy to have around . . . for quick relief from discomfort and pain. This is one of the several famous drug brands owned by Plough Inc., of New York, Memphis and San Francisco.

Relief of a different kind . . . relief from production plagues of various types . . . is one of the major reasons why Plough Inc., like many leaders in other fields, use Pneumatic bottling equipment. They know, from experience, they'll have fewer bottling hold-ups and headaches with Pneumatic equipment doing their cleaning and labeling. And they value Pneumatic's "lower cost per container" operation — natural result of Pneumatic's design and engineering specialization. Invariably the most careful, the most profit-minded buyers of packaging and bottling machinery are the best Pneumatic customers.

PNEUMATIC SCALE CORP., LTD., 70 Newport Ave., Quincy 71, Mass. *Also: New York; Chicago; Dallas; San Francisco; Los Angeles; Seattle; Leeds, England. Canadian Division: Delamere & Williams Company, Ltd., Toronto.*



Installation of Pneumatic labeling and air cleaning units in production of St. Joseph Aspirin in the modern plant of Plough Inc.

★ PNEUMATIC

Packaging and Bottling Equipment

the discard. We have thrown ourselves squarely into the power politics and the power wars of Europe, Asia and Africa. We have taken the first step upon a course from which we can never hereafter retreat. . . . If we stand any show, it will be from pursuing this new revolutionary foreign policy to the last limit with swiftest speed. I shall vote hereafter accordingly, but only because the Senate on this historic night has committed America to these illimitable obligations. Our fate is now inseverably linked with that of Europe, Asia and Africa. We have deliberately chosen to sit in on the most gigantic speculation since Time began."

Automation

It has often been remarked that we are an enthusiastic people. We like new things and new ideas; we even like old ideas and old things provided they are given a new catch-name and made to appear original. Automation is such a catch-name. Already it is catching on like wildfire. Millions will be wasted because of it. Already there is an automation magazine, through which its publishers will be able to sell the same advertisers additional space to cover the same fields. An automation trade association will soon be formed—if indeed it hasn't been already. One writer on the subject already is arguing for a new language especially tailored for this *new* science!

He could be right. Names like "servo" sound interesting and mysterious. How is your "amplitude response for harmonic input" or your "velocity step function" or your "polar frequency response." What do you know about digi-coders? Feedback? Inductosyn? Ultra-viscoson?

Man, you ain't heard nothin' yet!

Soon the following dialogue will be taking place daily all over the country. The scene will always be the same and the actors too. The scene, the office of Mr. Brasshed, the president, and the actors, Mr. Brasshed and Joe Catchall, the plant engineer.

"Say, Joe. Have we got any servos in the plant?"

"Servos? What are they?"

"Good God! You mean to tell me we got no servos after all the dough we waste in the engineering department? How do we stand on automation?"

"I don't know. What is it?"

Do you have the nerve to stand there and ask me what automation is? You've got a bunch of engineers sitting all day on their fat backsides drawing crossword puzzles and nobody knows a damn thing about what's going on. Why, when I took over this job twenty years ago we didn't have any engineers; now you've got a dozen—though God knows what for. None of them knows anything. Not even you. While you fiddle around with do-dads, I'll bet our competition is loading up on servos and automation. We're forty years behind the times in our plant—in spite of all the so-called engineers we waste money on. What a mill-stone around my neck."

"I'm sorry boss. This automation thing must be new. I'll look into it. Where did you hear about it?"

"I read about it in Fortune. Of course it's new. Now I want automation all over this place. Get rid of that bunch of dummies you've got and get some automatons around the plant. Servos! . . . I got it—a new selling slogan! "Servos for service!"

Joe Catchall sneaks out while Mr. Brasshed sits in a glassy-eyed trance contemplating his wonderful new slogan.

There is nothing new about automation. It has been going on ever since the beginning of the industrial revolution. Every improvement made on a machine is part of the process of automation; every new invention is another step. Ever since the first mechanical engineer was graduated a hundred years ago the process of automation has been going on. That's what engineers are for—all of them: mechanical, electrical, chemical. The so-called new twist is that machines are operated and controlled by various types of instruments, electronic devices and punched tapes. Instrumentation is not new; neither are the punched tapes. The Jacquard loom invented 150 years ago was controlled by a punched tape. Thirty years ago I worked for Frank J. Sprague (inventor of the electric motor) when he devised an animated electric advertising sign which was controlled by a punched tape.

But we are enthusiasts; we get excited about new slogans. And the danger is that millions will be wasted in attempting to make automatic, operations that are too infrequent in occurrence and too low in volume to warrant the investment in automatic control equipment. Out of the hundreds of thousands of plants in this country only a few make identical articles hour after hour day in and day out, and these are subjects for complete mechanization and mechanical control. In fact most of them are automatic now or very nearly so. I am connected with a relatively small chemical plant that is almost automatic. Only one product is made and we make it continuously.

The saving grace about the consultants who call themselves "automation engineers" is that unlike the efficiency experts and the so-called management engineers, they must actually be engineers, trained and broadly experienced, and not a bunch of salesmen.

Personality Testing

Off and on for the past several years I have taken pot shots at personality testing, "bump reading" as I have called it, but "applied phrenology" is probably a better term. Many companies still believe in aptitude testing, I.Q. ratings, personality ratings and all the rest of the expensive gibble-gabble. Long ago, when one of my clients fell hook, line and sinker for aptitude testing, he found that his star salesman was rated as below par as a salesman! Since then I have been skeptical of all this modern mumbo-jumbo that management engineers sell at such a high price.

But my skepticism brought criticism from many of

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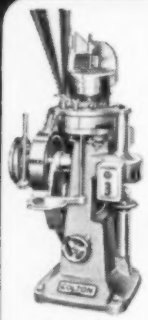
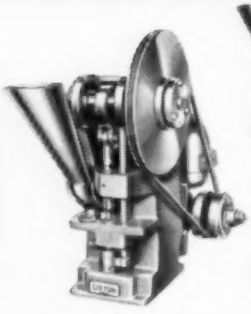


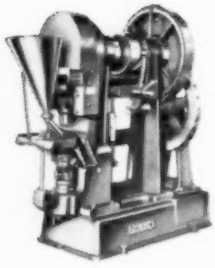
TABLET PRESSES. Single Rotary—Nos. 216; 240; 250; 270. Up to 1150 tablets per min. Up to 2" tablet dia.

TABLET PRESSES. Double Rotary—Nos. 227; 233; 241; 260. Up to 2900 tablets per min. Up to 1⅜" tablet dia.



TABLET PRESS. Single Punch. Bench Type — No. 301. Up to 65 tablets per min. Up to ½" tablet dia.

TABLET PRESSES. Single Punch—Nos. 320; 330; 340. Up to 120 tablets per min. Up to 1¼" tablet dia.



TABLET PRESSES. Single Punch, Heavy Duty—Nos. 345; 350; 360. Up to 85 tablets per min. Up to 3" tablet dia.

TABLET and CAPSULE COUNTERS—No. 715 Single; No. 705, 5-Bottle; No. 710, 10-Bottle.

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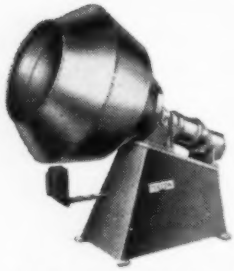
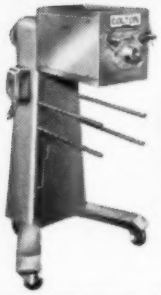
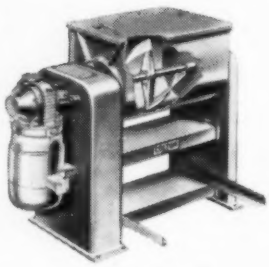


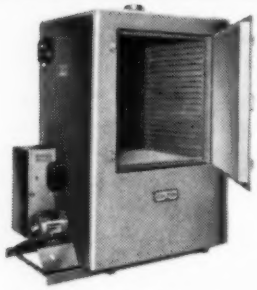
COATERS: POLISHERS: BLENDERS:—No. 36. Laboratory Size; No. 26. Bench Size; No. 16. Standard Size; No. 56. Tilting Type; No. 46. Large Blender.



GRANULATORS. Dry—No. 544 Twin. Also, Wet Granulators No. 551, 4-Blade; 561, 6-Blade.



MIXERS. Dry—No. 617, 17 Gal.; No. 636, 36 Gal.; No. 685, 85 Gal.; No. 695, 175 Gal. Also, Paste Mixers.



DRYING OVENS—No. 1018, 10-Tray Lab.; No. 2030, 20-Tray Cabinet; No. 4030, 40-Tray Truck.

STAINLESS STEEL STOCK POTS & TANKS—All types, open and closed. All sizes up to 5,000 Gal.

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MULTIPLE SPOUT LIQUID FILLERS—32 to 480 fills per min. Up to 4 Fl. Oz. 4, 6, 8, 12 nozzles.

CREAM AND PASTE FILLER—No. 130. Hand Operated. Up to 30 tubes or jars per min. Up to 1" x 5½" tube size, with single stroke.

TUBE FILLERS, AND CLOSERS, AUTOMATIC—Nos. 175; 180; 190. Up to 100 tubes per min., liquid to heavy paste.

TUBE AND JAR FILLERS, GEAR OR WORM, POWER DRIVEN—Nos. 110; 140; 150. Up to 50 fills per min. Up to 2"x11" tube size.

TUBE FILLER, CLOSER, & CRIMPER, LIQUID & PASTE—No. 113. Up to 40—6-Fl. Oz. fills per min.

TUBE CLOSER, HAND OPERATED—Nos. 440; 450. Up to 20 tubes per min., 2½" x 10" max. size.

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my enthusiastic clients; they said I was weak in personnel matters and old fashioned in my views.

I never had the opportunity to establish the validity of my skepticism, but in the September issue of Fortune, William H. Whyte, Jr., did it for me in an article, "The Fallacies of Personality Testing." If you haven't read the article; by all means do so. I regard it as one of the most important business articles ever written because too many top management people are hypnotized with the idea that all you have to do to pick a top flight executive is to have his bumps read by one of the practitioners of this modern pseudo art. The sum and substance of Whyte's article is that he arranged with thirty of the top flight corporation presidents of this country—men who are known for their exceptional business ability—to take epitomized tests, such as the Minnesota Multiphasic Personality Inventory, Thurstone Temperament Schedule, A-S Reaction Study, Supervision Tests, Practical Judgment Tests, etc., etc. As a result it appears that American industry is being run by a bunch of morons, because they didn't do so well. As Whyte puts it, "If the tests were rigorously applied across the board today half the most dynamic men in business would be out walking the streets looking for a job."

Whyte's article repeats the tests and gives you an opportunity to rate yourself. I took the tests and answered all the questions honestly and with equal honesty computed my rating. Apparently I am somewhat less intelligent than a chimpanzee. I realize that a pretty good argument could be put up on the basis that I look like one, but I'll be damned if I ever thought I think like one.

Like so many other expensive enthusiasms that American business waste money on, personality testing and aptitude testing have some merit when evaluated with common sense. I think children can be analyzed fairly accurately. But the adult, with his accumulation of experience, education, prejudices, intuitions, predilections, habits, vices and virtues is something else again. The E.V.P. of a famous corporation—an M.I.T. graduate incidentally, who in school and out, and in the Navy as well, had been exposed to all manner of "scientific tests," offered to bet me a case of Scotch that if he knew beforehand what the job was, he could take any test or combination of tests and qualify for that job. I believe him. I still believe in the old fashioned way of sizing up people. Talk to them at length. Look at them carefully, critically, especially when they are asking questions. Follow your intuition.

Arthur Meggett

In Hamilton, New York, you will find a guy named Arthur Meggett, who is an architect, an industrial designer and a damned good engineer. If you want to build a house, a school, a church or a factory anywhere in New York State, Art is your man. Unlike many, if not most architects, Art is practical. He is also imaginative and constructive. I know he is sound on plant design because he has worked with me on many plant projects for the past twenty years. If you have been reading this column very long you will appreciate that when I give a plug to an architect he must be good. Art is.

The following information is supplied by manufacturers of the equipment described and claims made below by these manufacturers are passed along for what they are worth. Presentation of such notice in this department is not to be taken as endorsement of the claims or of the equipment.

Universal Recording Balance

A bulletin which illustrates and describes an entirely new and unique Universal Recording Balance has just been published by the Sharples Corporation Research Laboratories, Bridgeport, Pa.

The bulletin describes the principle of operation and functioning of this precision instrument which is specifically designed for the observation and recording of small, rapidly changing forces with respect to time. Twelve important uses of the Universal Recording Balance are listed, such as the observation by direct weighing, of the action of gases on metals at high temperatures, and the study of evaporation of solvent mixtures or solvents from paint film. Eight distinct advantages of the Universal Recording Balance are discussed.

Requests for copies of this bulletin will receive prompt attention if addressed to The Sharples Corporation Research Laboratories, 424 W. 4th St., Bridgeport, Pennsylvania.

Material Handling

A new, twenty-eight page treatise, entitled, "Why the Small Fork Truck?", by Nathaniel Warshaw, manager of the Materials Handling Division of Market Forge Company, Everett, Mass., shows how small and medium-sized plants can compete with big business in materials handling efficiency. This book may also serve as a text for teachers and students and will be a useful training aid in industry to provide a better understanding of the design and function of small power trucks.

A unique study, "Why the Small Truck?" analyzes the space, time and labor factors involved in small plant operation and suggests fundamental solutions, derived from Mr. Warshaw's own thirty years of experience in the design and manufacture of materials handling equipment, and based on actual results of their application in plants throughout the world.

"Why the Small Fork Truck?" reflects a deep understanding of management and production problems. It deals with the specific requirements of small and medium-sized plants for efficient handling of materials. Illustrations, figures and charts show features of design, construction and performance of small power fork trucks for handling materials, and also serve as refer-

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A JOB TO BE DONE . . .
rely on this workhorse, a machine that never seems to get overloaded . . .

Kiefer CADET MODEL
VARI-VISCO
CONVEYOR TYPE
FILLING MACHINE

Results are simply amazing with this junior member of the famous Vari-Visco family. And not only VOLUME but ACCURACY are at a lively rate—this filler meets the closest specifications.

The turn of one handwheel sets filling quantity . . . another — the speed, a matter of mere seconds for your selection.

Equipped with container lift for "bottom up" fill . . . gives viscous materials a solid pack or avoids splash with all liquids. Automatic feed and discharge conveyor.

No. 30 MONOCELL SHEET FILTER

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ence sources for the selection of equipment of the proper size, weight and capacity.

The twenty-eight page booklet is written in an interest-holding, non-technical style, yet it displays text-book authority for extensive library use by top management, production and materials handling engineers, time study experts, teachers and students. It fills the need for a fundamental study of the materials handling problems of small and medium-sized plants, and rates heartiest congratulations to Nat Warshaw for a successful effort to show the way to new production efficiency for the little fellow who is the backbone of American industry.

Now on the press for a limited edition, "Why the Small Fork Truck?", by Nathaniel Warshaw, may be obtained by writing to Materials Handling Division, Market Forge Company, Everett 49, Massachusetts.

Miniature Rotary Filling Machine

The MRM Company, Inc., announces the development of a new liquid filling machine with a novel feed arrangement, which permits the filling of containers of any shape or size without changing the feed setup.

This machine was designed particularly for those manufacturers of liquid products such as perfumes and toilet preparations, who do their packaging in a wide variety of containers. Among such containers will invariably be odd shaped types that cannot be properly handled by the ordinary conveyor and star equipped machine.

Where skilled help is scarce, this new machine will provide reliable, automatic filling utilizing present personnel. Also, where production is based largely on short runs, thereby preventing the use of mass production lines, because of the costly changeover time involved, the MRM universal feed machine now allows fully automatic operation regardless of the shape of the container or the length of the production run.

The feed arrangement of the new machine consists of a series of flat plates mounted on a chain. The containers are fed on to these plates and are carried under the filling nozzles by the moving chain. Since the plates are permanently synchronized with the filling nozzles, all stars and guides are eliminated, and any shape or size of container is accommodated.

The machine will handle all types of containers from fractional ounce to 16-ounce sizes, at production speeds up to 75 a minute. MRM Company, Inc., 191 Berry Street, Brooklyn 11, N. Y.

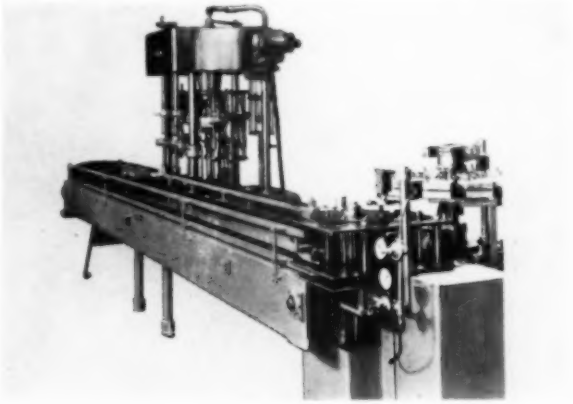
High-Speed Filling and Sealing of Plastic Containers

Latest development of the special packaging equipment division of the MRM Company, Inc., is a machine which fills and heat-seals the closures of "Bracon" plastic containers manufactured by the Bradley Container Corp. of Maynard, Mass.

Designed for the filling of all types of liquid products, its fully automatic, continuous operation allows production speeds of up to 120 a minute. In operation, the containers are fed into specially designed holders on a chain-driven conveyor, which carries them into a 12-station, rotary filling unit. There they are filled by gravity, vacuum, or pressure, as desired. The entire filling mechanism is above the conveyor, so that the floor is kept clear of encumbrances which might interfere with cleaning. After filling, the containers are fed into a 12-station, rotary sealing unit, whose speed is synchronized with that of the filling unit. There, a heat seal is applied, welding the base plate to the Bracon bottle.

All parts of the machine which come in contact with the filling material are of stainless steel.

Mr. Herman Manas of MRM states that this equipment is available both for fully automatic or semi-



automatic operation, and high or low production requirements. It can also be furnished for heat-sealing of collapsible plastic tubes.

Inquiries may be directed to the MRM Company, Inc., 191 Berry Street, Brooklyn 11, N. Y., a firm with over 20 years of experience in the manufacture of filling, labelling and conveying machinery.

New Histological Freeze-Dryer

Research into the basic structure of living tissue, such as studies of cancer and brain tumors, will be stimulated and greatly facilitated by a new histological freeze-drying unit just introduced by F. J. Stokes Machine Company, Philadelphia, Pa.

The new Stokes unit dehydrates plant or animal tissue specimens under a vacuum of 0.1 micron at a very low temperature, well below the eutectic point for biological materials. This prevents oxidation, and also prevents any movement of the individual chemical components of the cells, so that they retain their original shape and form and orientation. The freeze-dried specimen is then imbedded in paraffin, if desired, while still under vacuum. It can then be microtomed (sliced thin) or otherwise prepared for examination under the microscope without fracturing.

NO OTHER FULLY AUTOMATIC LABELER CAN

You'll find them only in

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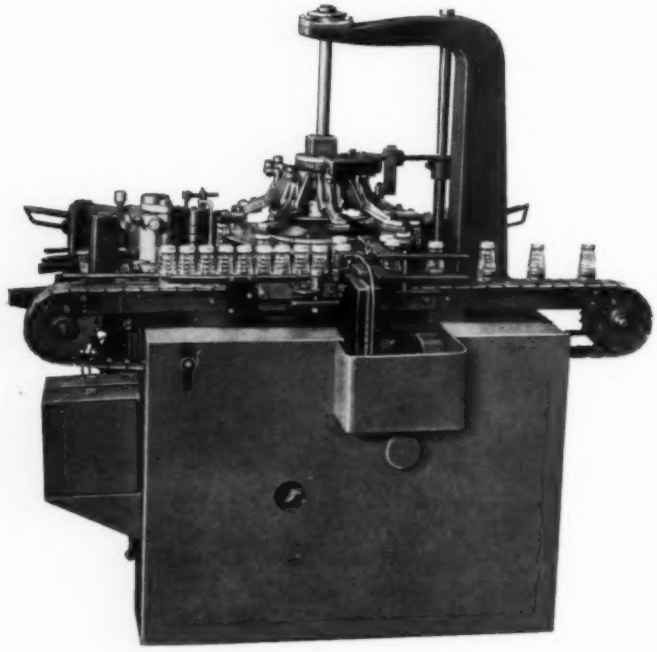
GIVE YOU ALL THESE Extra ADVANTAGES



1. Handles oval, square, round and tapered shapes.
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3. Uses vacuum principle of label handling to assure perfect register and minimum glue attention.
4. Effective circulating glue system, - with micro glue control to prevent glue smears on containers.
5. Requires NO OPERATOR.
6. Petty-Cash Change-parts.
7. Clamps containers into position **prior** to moving container toward labeling station, to avoid faulty label register.
8. Change-over almost as quickly and simply as the Pony Labelrite.
9. No label-feeding unless incoming containers signal their approach.
10. Self-cleaning glue system,

The PONY EXPRESS is a logical development incorporating all the precision features which have made an unprecedented reputation for the Pony Labelrite. Being fully automatic, the FULL rated capacity (70 per minute) is available for sustained production.

Here, for the first time, is an automatic which is **not** "single-purpose", or restricted to a greatly limited range of work,—usually the case with ordinary automatic machinery.

We'll gladly arrange a demonstration!

539 ***Send in sample containers with labels for accurate details!***

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The new histological freeze-dryer was developed by Stokes in cooperation with Dr. Ernest W. Retzlaff of the University of Michigan to meet a growing need for equipment of this type as a result of increasing activity in tissue research.

Its design provides great flexibility in operation, and permits many different histological and histo-chemical techniques to be carried out with it. Among the applications for the new unit pointed out by Dr. Earl W. Flosdorf, a pioneer in freeze-drying technology and now Stokes' director of research, it will be extremely useful in determining the location of individual chemical constituents within the structure of a single cell, and may thus be expected to contribute greatly to experimental work on the nature of living matter.

The unit is compact, easily operated, and incorporates many features that simplify handling of the specimens and save a good deal of experimental time. It is said that the new Stokes freeze-drying unit accomplishes in 10 hours or less, work that has previously taken as much as a week or more of painstaking manipulation.

The tissue specimen is frozen by immersing it in isopentane which has been chilled to approximately −150° C. by liquid nitrogen. Meanwhile the paraffin has been melted, de-gassed, and re-solidified. The frozen specimen is then laid on the paraffin and both are placed in the drying chamber which is then surrounded by a bath of ethyl oxalate slush at −40° C. chilled with dry ice. The heating effect resulting from the difference in temperature of the frozen specimen and the ethyl oxalate bath causes the moisture in the specimen to sublime and pass off to the condenser. The condenser is chilled with liquid nitrogen.

Drying under vacuum is continued for nine hours. The paraffin is then melted, without breaking the vacuum, and the specimen, now thoroughly dried, sinks into it. The paraffin is again re-solidified and the specimen brought back to room temperature. Only then is vacuum broken.

The self-contained unit, with its own vacuum pumping system consisting of a water-cooled oil diffusion pump and a mechanical fore-pump, is housed in a compact cabinet 48 in. high, 54 in. long and 24 in. wide. Weighing only 1,000 lbs., it is mounted on casters so that it can be easily moved to any desired location. When electrical and water connections are made, and oil has been supplied to the mechanical fore-pump, the unit is ready to go to work. The diffusion pump is shipped with its oil already sealed in.

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The machine is equipped with an attachment that automatically raises the glue roller in the event the production line should stop. This precautionary device prevents the adhesive from building up on the bottle directly underneath the glue roller. When the line is once again in motion the glue roller automatically drops down into position and resumes application of the precise amount of adhesive immediately.

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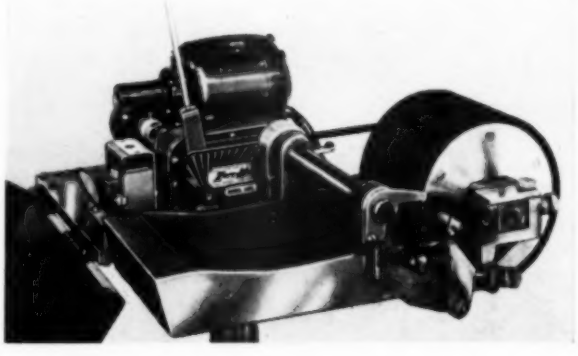
A variable speed control provides perfect synchronization with the speed of the bottling line. The turning of the glue roller is instantly adjustable to the desired speed of the bottling operation. To facilitate cleaning of the Potdevin bottle top coater, the machine was designed to readily remove the entire unit. The roller and the tank can be slid off its mounting and placed in a pail of solvent or under a water faucet, depending on the type of glue used.

To protect the machine from infiltration of dirt or foreign matter into the glue pot, a special guard is provided that covers the entire unit. The guard also imparts a neat appearance in keeping with the trend to attractive production equipment design. Potdevin Machine Co., 285 North Street, Teterboro, New Jersey.



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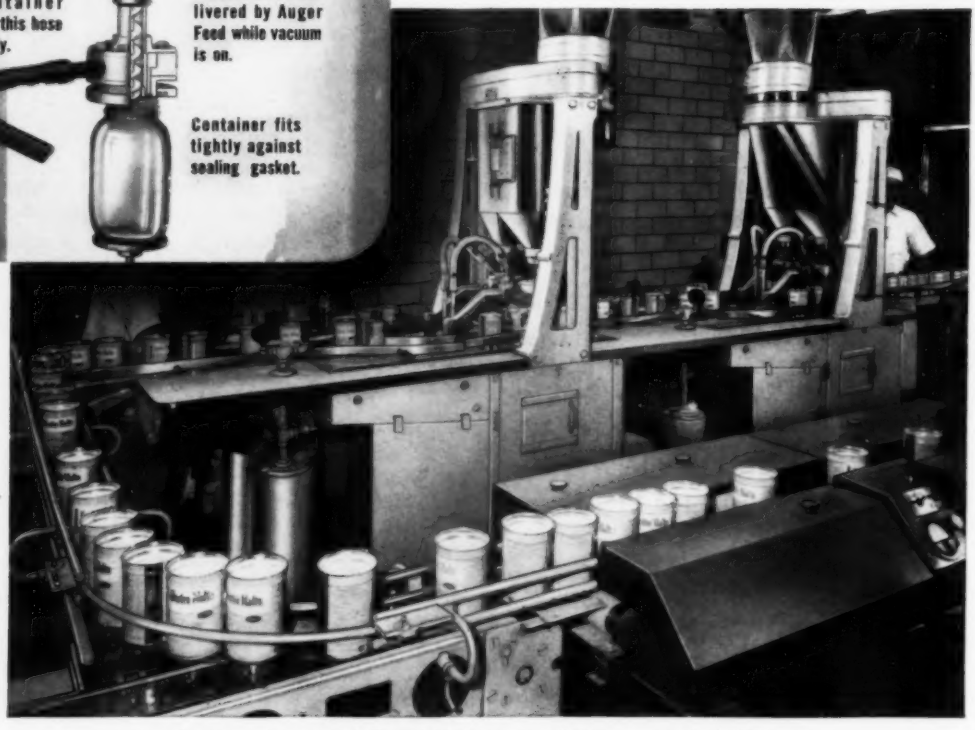

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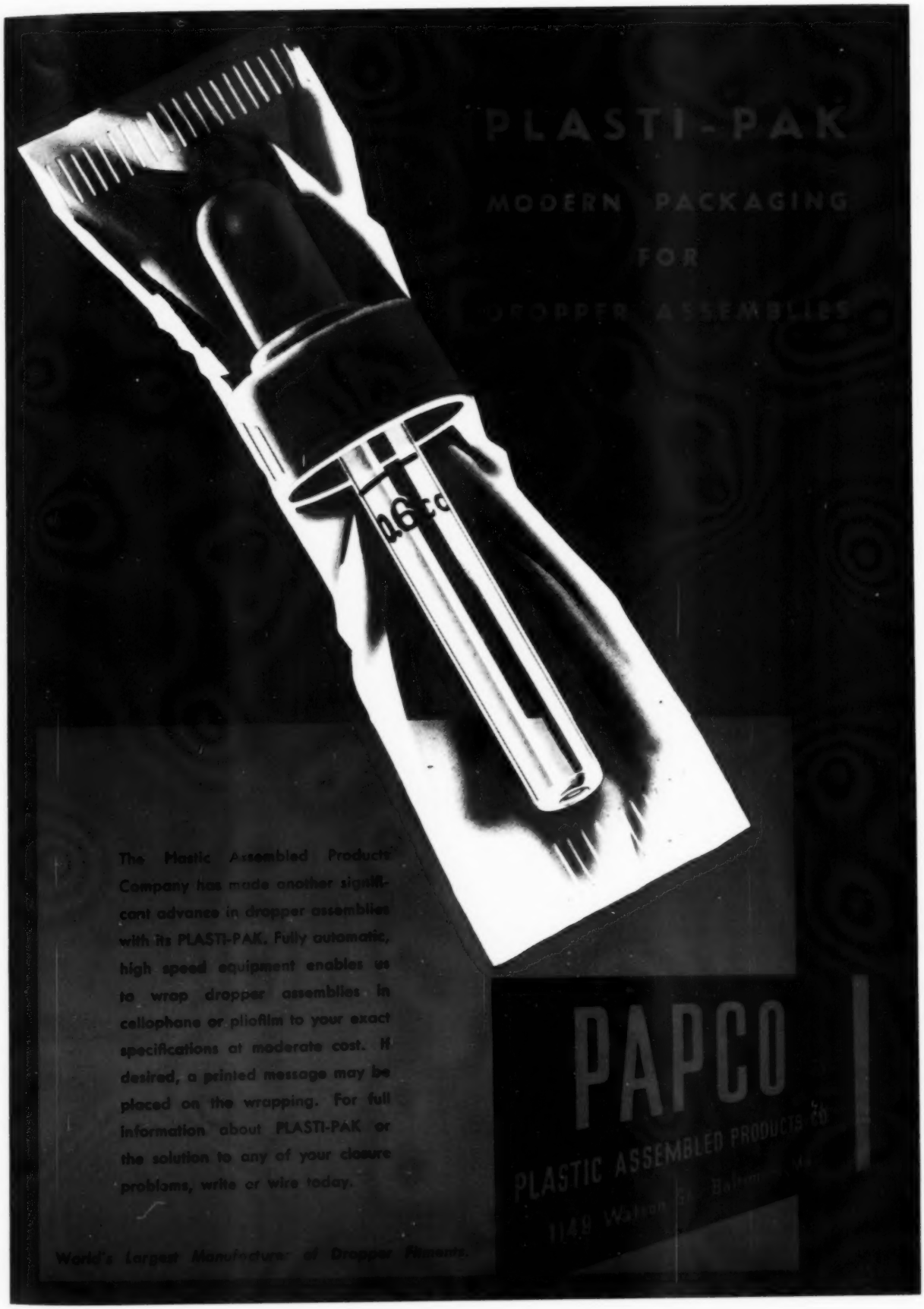
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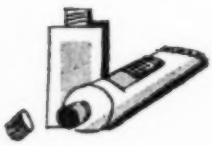


Advancing Therapy

Antibiotic Therapy for Bronchitis and Asthma

The results of long-term antibiotic treatment of 135 adults and 109 children with chronic bronchitis and infectious asthma have been reported by W. Finke (*Antibiotics & Chemother.* 4: 319, 1954). Penicillin was the mainstay for treatment in this study, the parenteral route being replaced more and more by oral and aerosol therapy. The daily dosage of oral penicillin taken on an empty stomach varied between 1,000,000 and 3,000,000 units in the beginning of treatment, and 500,000 to 1,000,000 units later on, and was determined more by the severity of a given case than by the patient's age. Penicillin aerosol, which provides high local concentration, was given to most adults and older children. Two hundred thousand to 500,000 units crystalline powder or soluble tablets, dissolved in from 1 to 2 cc. of a nonirritating detergent, were inhaled one to three times a day. An inexpensive, simple aerosol technic, using a handpump with a plastic air reservoir as the source of pressure, usually proved adequate for home treatment.

In many instances as little as one daily inhalation or one oral dose of penicillin kept the infection under control over prolonged periods and, therefore, proved adequate for maintenance treatment following more intensive therapy. However, a combination of both methods, and even parenteral penicillin in addition, often were necessary, especially in the beginning of treatment and during exacerbations. Therefore, when used alone, excessive doses of this antibiotic sometimes could not be avoided. Hypersensitivity to penicillin in some patients, the greater risk of complications from large doses, as well as the search for more effective therapeutics, led to an increasing use of newer antibiotics, either alone or in combination with penicillin. Streptomycin or dihydrostreptomycin was given parenterally or by aerosol in doses rarely exceeding 0.5 Gm. per day. Chlortetracycline, chloramphenicol, and oxytetracycline were used orally.

The data obtained indicate that, in general, better results could be achieved in children than in adults, and that the improvement was more complete in patients with chronic bronchitis than in those with infectious asthma. These differences can be explained by the higher incidence of advanced disease among adults, and by the prevalence of persistent bronchial obstruction and emphysema in both children and adults with infectious asthma.

In Finke's opinion the experience gained in the course of this seven-year study shows that prolonged antibiotic therapy of bronchopulmonary suppuration, which is the underlying condition in chronic bronchitis and infectious asthma, can rehabilitate even advanced cases and cure early ones. This indicates the rationale of the earliest possible termination of respiratory infections from which chronic disease may develop.

Trypsin Debridement in Dentistry

In investigations made by A. M. Olinger, Jr. (*J. Am. Dent. Assoc.* 49:166, 1954) enzymatic débridement with trypsin as an adjunct in the therapy of periodontal disease was employed in 32 clinical cases. The cases included four of gingivitis, four of Vincent's infection, 20 of periodontitis and four of periodontosis. The method found most satisfactory was to apply the trypsin with saturated cotton dressings. Of the dosages tried, a concentration of 125,000 Armour units of crystalline trypsin in 0.4 cc. of Sorensen's phosphate buffer solution was the most effective. The removal of slough and necrotic debris was an aid in the promotion of normal physiology of periodontal tissues. Debridement was complete within 10 to 20 minutes. Inflammation was reduced by tryptic action, and the rate of tissue repair was accelerated. Dental structures were unaltered by trypsin, and no systemic or undesirable local effects of any consequence were observed. Trypsin had no action on dental caries, and calculus deposits were unaffected. Trypsin did not reduce the depth of periodontal pockets unless the soft tissue portion of the pocket was necrotic.

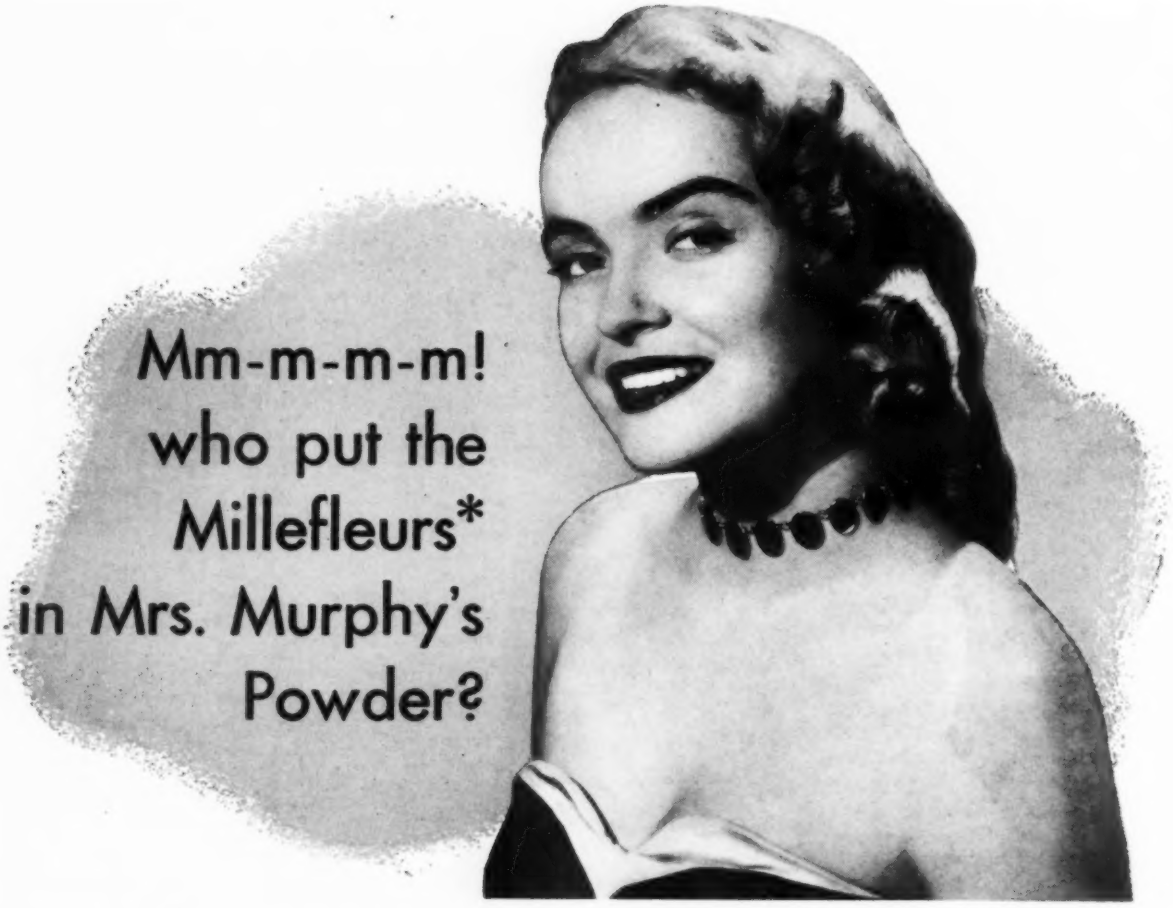
Olinger believes that when used according to the methods described, trypsin affords, to a much greater extent than heretofore possible, a means of supplementing the removal of debris associated with infected periodontal lesions.

Vitamin C in Hepatitis

The intravenous administration of ascorbic acid has been found of value by H. Baur and H. Staub (*Schweiz. Med. Wochenschr.* 84:595, 1954) in the treatment of 11 cases of epidemic hepatitis. The dosage was 10 Gm. of ascorbic acid in one liter of normal saline daily for five days. It is claimed that this accelerated the fall in serum bilirubin, shortened the period of urinary excretion of bile pigments, facilitated gain in weight and shortened the duration of the illness. No side-effects were encountered from the use of ascorbic acid. Two possible mechanisms for this action of ascorbic acid are discussed: that it exerts a viricidal effect, and that it acts indirectly by affecting the disturbed metabolism of the disease.

Combined Therapy for Diarrhea

A. M. Hand, W. T. McLean, Jr. and J. N. Etteldorf (*J. Pediat.* 44:407, 1954) report that of 100 infants and children with mild, moderate and severe diarrhea caused by infections with *Shigella paradysenteriae* or of unknown cause, 50 were treated with a combination of chlortetracycline (Aureomycin) and triple sulfonamides (sulfadiazine, sulfamerzine, and sulfamethazine) in a liquid preparation (Aureomagma). The dosage of Aureomagma was calculated to supply 12.5 mg. of chlortetracycline and 50 mg. of the three sulfonamides per kilogram of admission weight per 24 hours. The original preparation was diluted 1:10 and administered at six hour intervals. Vomiting occurred in only one patient after the administration of Aureomagma, although some of the patients had vomited before their admission. The other 50 patients served as a "comparison" group and received antibiotics (penicillin, oxytetracycline, chlortetracycline, streptomycin) and chemotherapeutic agents (sulfadiazine) singly or in combination. The combination of



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chlortetracycline and the three sulfonamides was evaluated according to the following criteria: (1) reversal of positive stool cultures, (2) influence on the duration and severity of diarrhea, (3) requirement for extended parenteral fluid therapy, (4) reduction of fever, (5) length of hospitalization, (6) blood sulfonamide levels, and (7) undesirable side-effects. By these standards, the combination of chlortetracycline and the three sulfonamides was superior to the chemotherapeutic and antibiotic agents used in the comparison group when the rest of the treatment was similar.

Erythromycin in Diphtheria

In a study of the usefulness of erythromycin in the treatment of clinical diphtheria, J. F. Blute, Jr. (*New England J. Med.* 251:70, 1954) administered this antibiotic to three patients with acute pharyngeal diphtheria and to one diphtheria carrier. In all four patients the organisms were cleared from the nose and throat within 24 hours, and repeated cultures were negative for *C. diptheriae* during the period of hospitalization. Two patients with acute disease received antitoxin in addition to erythromycin. The patient with the mild case and the diphtheria carrier were treated with erythromycin alone. Three of these patients received the erythromycin by mouth. The fourth required intravenous administration.

From these observations, Blute concludes that erythromycin appears to be effective in rapidly clearing diphtheria organisms from the throat. Moreover, the availability of an intravenous preparation increases its usefulness in the very sick patient. Hence, erythromycin is advocated as an adjunct and not as a substitute for antitoxin in acute diphtheria.

Vitamin A Levels in Dermatology

It is pointed out by K. D. Lahiri and F. J. Scandrett (*Indian Med. Gaz.* 89:31, 1954) that one of the most important functions of vitamin A is its influence in maintaining the structural integrity of epithelial cells. Changes in the skin are among the earliest signs of vitamin A deficiency. Lahiri and Scandrett studied the serum vitamin A concentration in cases of ichthyosis, nummular eczema, Besnier's prurigo, neurodermatitis, and alopecia areata. They detected a definite lowering of vitamin A levels in the serum of patients with ichthyosis and nummular eczema, whereas in cases of Besnier's prurigo, neurodermatitis, and alopecia areata the serum vitamin A concentration was within the normal range. Encouraging results have been obtained with vitamin A therapy in ichthyosis and in nummular eczema by one of these workers. Other dermatological conditions in which vitamin A therapy has been found effective by these and other investigators include leukoplakia, kraurosis vulvae, pruritus vulvae, brittleness of the nails, chronic hyperkeratotic lichen simplex, benign chronic pemphigus, alopecia, cavities, and macular pigmented lesions observed in patients subsisting on diets low in animal proteins.

Cortisone Ointment for Pruritus Ani

Having observed that patients receiving cortisone therapy for various conditions frequently obtained relief from chronic pruritus ani, C. F. Baumeister (*J. Lancet* 74:89, 1954) employed an ointment of 2 cc. (50 mg.) of cortisone suspension with enough aqueous base to make a total of one ounce for treatment of pruritus ani. Palliative results were obtained in 70 per cent of the patients. In cases with an element of infection, ointments containing bacitracin, polymyxin, and zincundate (Desenex) were used in addition. The hard, glazed, varnish-like coating found in advanced cases must be removed by suitable softening ointments. The cortisone ointment was used in the more stubborn cases that had proved refractory to other measures.

Phenylbutazone in Gout

An evaluation of the effects of phenylbutazone (Butazolidin) has been made by H. P. Johnson and his associates (*New England J. Med.* 250:665, 1954). They report that phenylbutazone is clinically effective in the control of acute gouty arthritis and in the suppression of chronic gouty arthritis. Toxicity was of no consequence in the short-term treatment of 10 patients with acute gouty arthritis. Undesirable toxic reactions were frequent in long-term use, however, occurring in nine of 16 patients with chronic gouty arthritis.

The mode of action of phenylbutazone remains unexplained, but certain metabolic effects appear significant. The drug decreases the uric acid concentration in the serum while reducing the excretion of most of the urinary constituents — namely, creatinine, 17-hydroxycorticoids, 17-ketosteroids, sodium, potassium, chlorides and uric acid—as well as lowering the urinary volume. Adrenocortical activation is not included as a significant factor in the mode of action of this drug.

Despite its favorable therapeutic effects, the investigators believe that the potential toxicity of phenylbutazone should limit its use to cases of gouty arthritis that are resistant to other established forms of treatment.

Pyridoxine with Isoniazid in TB

It is pointed out by J. Unger, E.G. Tomich, K. R. Parkin and P.W. Muggleton (*Lancet* 2:220, 1954) that side-reactions have been reported in man after isoniazid treatment and in animals after prolonged treatment with high doses of the drug. Pyridoxine (vitamin B_6) in suitable doses appears to counteract the side-effects of isoniazid in animals. Pyridoxine does not interfere with the direct anti-tuberculous activity of isoniazid *in vitro* or in infected mice. Hence it is suggested that pyridoxine could be tried without adverse effect in the isoniazid treatment of patients who show signs of intolerance to the drug. From the *in-vitro* study and the tests on infected mice it appears that pyridoxine administered for this purpose to patients is unlikely to have an adverse effect on the antituberculous action of isoniazid.

Penicillin & Sulfas for Respiratory Infections

In the study reported by J. W. Daly (*Antibiotics & Chemother.* 4:687, 1954) a combination of dibenzylethylenediamine dipenicillin G and triple sulfonamides has been used for the treatment of upper respiratory infections of presumably mixed etiology. The penicillin salt has been shown to be reliably absorbed when given by mouth, while the triple sulfonamide component has demonstrated its capacity to produce and maintain therapeutically effective blood sulfonamide levels. The combination, given as tablets or as an oral suspension, was administered to 50 patients with acute upper respiratory infection. Satisfactory results were observed in 47 cases. The preparations were well tolerated; no instance of sensitivity was noted, and in no case was it necessary to discontinue therapy because of adverse side effects. No instance of a secondary purulent infection was encountered in 50 unselected cases of acute upper respiratory tract infection.

Animal Health

Zoonoses

It appears that the term "zoonoses," which denotes diseases of animals transmissible to man, will become more familiar in the future. Bubonic plague, rabies, bovine tuberculosis, brucellosis, anthrax, leptospirosis, anthropod-borne virus encephalitides, Q fever, hydatidosis, salmonellosis, and tularemia are important zoonoses in large areas of the world. As pointed out by S. W. Goldstein (*J.A.Ph.A.*, Pract. Ed. 15:423, 1954) it is evident that the prevention and eradication of zoonoses in human beings can be accomplished in large part by control of these diseases in animals. He cites a monograph published by the World Health Organization which mentions more than 80 zoonoses. It indicates that 10 or 15 are most important to European countries, and devotes special attention to five of these diseases. The report states that bovine tuberculosis is responsible, in some countries, for more than 10 per cent of all cases of human tuberculosis; that brucellosis can be ruinous for agricultural economy besides causing a debilitating disease in the human; that leptospirosis, the scourge of rice-growing areas, also affects butchers, millers, farmers, and owners of pets (dogs); that Q fever is frequent among butchers, shepherds, and veterinarians; and that rabies is still a serious problem in many parts of the world.

The problem of zoonoses, says Goldstein, is naturally more serious in the population that has more contact with animals. Children living on farms can contract bovine tuberculosis by consumption of raw milk or even through the respiratory tract. Brucellosis, also known as melitococcus, undulant fever, Maltese fever, or Bang's disease, according to the strain of microorganism involved, is very frequent among cows, pigs, goats, and sheep; and is usually transmitted to man through raw milk or fresh cheese. Among the animal population it causes abortion and sterility. In man, the sulfonamides and antibiotics have greatly aided the manner of treatment of the afflicted. Leptospirosis, also known as marsh fever or seven-day fever, is a serious human infection which may resemble infectious hepatitis and is sometimes fatal. The parasite, found in rodents, is transmitted to man through mud, stagnant water, and improperly treated water in swimming pools. Good results in the treatment of the disease are obtained with penicillin, streptomycin, and aureomycin.

Oral Stilbestrol for Fattening Cattle

W. Burroughs and his associates (*Science* 120:66, 1954) have found that the placing trace amounts (e.g. 5 and 10 mg. per animal daily) of diethylstilbestrol in the feed of fattening steers increased live-weight gains by as much as 35 per cent over control animals not receiving this substance and reduced feed costs per unit of gain as much as 10 per cent. No reduction in the fatness of the cattle or the quality of the meat occurred in the chemically treated animals compared with controls. Moreover, the results obtained in these studies indicate that oral administration of diethylstilbestrol produces the desirable effects of pellet implantation without any of the undesired side effects. An important advantage is the ease with which the material can be supplied to cattle by incorporating it in their feed. In addition the material can be easily removed from the rations of cattle should errors be made in the amounts administered, or should other unforeseeable situations develop.

Phenothiazine for Internal Parasites of Cattle

During the past decade, note H. Herlech and D. E. Porter (*Vet. Med.* 49:103, 1954), free-choice administration of phenothiazine in salt and mineral mixtures has been employed extensively and, in general, successfully, for the control of gastrointestinal parasites of sheep. However, comparatively little investigation has been made of the possible effect a similar regimen might have on the helminthiases of cattle. An experiment covering a two-year period and involving 28 calves from four to nine months of age indicated that a regimen of free-choice administration of phenothiazine-mineral mixture effectively controlled the level of parasitic infection of the calves with *H. contortus* and *O. radiatum*. The program showed no significant effect on *O. ostertagi*, *T. axei*, *C. punctata* or *N. helvetianus*. The rate of consumption of phenothiazine ranged from 0 to 3 Gm. per head per day with the highest rate of consumption occurring during the warm spring and summer months, while consumption was negligible during the winter, apparently as a direct result of the feeding of supplements such as hay and grain. A base of mineral mixture for the phenothiazine appeared to be preferable to one of salt. This was a 1:9 phenothiazine-mineral mixture consisting of three parts each of salt, bonemeal, and crushed limestone, and one part phenothiazine, by weight.

Vitamin K for Cattle Hematuria

According to F. Debecker (*Alarms Diergeneesk. Tijdschr.* 22:269, 1953 through *J. Am. Vet. Med. Assoc.* 125:82, 1954), when vitamin K is given in time, it is practically a 100 per cent cure for essential hematuria in cattle. About 50 per cent of the cases start anew after four months, but they soon recover when given vitamin K. By testing a large number of animals, both sick and healthy, it was found that those which remained two years or more in an area where this condition is prevalent had too slow a coagulation of the blood due to a deficiency of vitamin K. This deficiency occurs gradually, probably because of a low vitamin K-production by the intestinal flora which is altered through a too acidic base (pH 4-6).

A secondary cause of this disease is a lowered vascular resistance in the blood network of the bladder, which may be due to a large quantity of oxalates or other mineral salts eliminated by the bladder; extreme temperature changes; chronic hemoglobinuria of piroplasmo-

sis; vitamin C deficiency; hormone change during pregnancy; or bladder infection. Regardless of the cause, the mechanism of the disease remains the same; once the hemorrhage starts it continues indefinitely. Vitamin K is definitely the etiological treatment of essential hematuria, and serves a preventive as well as a curative purpose—preventive in that it acts to alter the intestinal flora by base improvement.

Acetonemia Therapy

A new treatment for acetonemia has been reported by M. Lecomte (*Bull. Acad. Vet.*, Feb. 1954, through *J. Am. Vet. Med. Assoc.* 125:164, 1954); 20 cows, some associated with milk fever, receiving the therapy. For simple acetonemia, Lecomte used 50 cc. of a 20 per cent solution of acetylmethionine intravenously. He reports return of appetite and disappearance of ketones in the milk and on the breath within 24 hours. Only two cows required a second treatment, three days following the initial injection. When the acetonemia is associated with hypocalcemia, the following solution is used intravenously:

Calcium chloride solution, 50 per cent	**80 cc.**
Solucamphor	**10 cc.**
Adrenalin 1:1,000	**1 cc.**
Solution of methionine, 20 per cent	**50 cc.**

It is stated that the solution of methionine has also proved useful in the treatment of calcium-refractory cases of milk fever and is believed to be a valuable adjunct in this type of hypocalcemia.

Therapy for Cattle Respiratory Diseases

In discussing the therapy of respiratory diseases of cattle, G. E. Krill (*Vet. Med.* 49:328, 1954) observes that many antibiotics are available for treating these conditions. At times, due to tolerance factors, it may be necessary to employ more than one of these drugs, either alone or in combination. As a routine treatment a triple sulfonamide (sulfamerazine, sulfapyridine and sulfathiazole, four per cent of each) is employed at the rate of 1 to 1½ gr. per pound body weight. In cases where a suitable response is not apparent in 24 to 36 hours, an antibiotic is employed. Treatment is always continued two days, and in many cases for three. This schedule had proved almost 100 per cent in those uncomplicated cases that are treated early. For those complicated, stubborn or "late-get-to" cases Krill suggests a trial of one of the following measures: (1) penicillin (1500 to 3000 units per lb. wt.) in the chronic or subacute shipping fever cases where lung abscesses are suspected. *Corynebacterium pyogenes* is the chief offender in such cases. Penicillin is effective, (2) in cases of severe dehydration, give daily, by stomach tube, three to five gal. of water, milk with eggs, rumen culture and even alfalfa meal, (3) in cases of severe pulmonary edema attempt is made to remove excess fluid from the lungs, administering 50 per cent dextrose intravenously, usually 1,000 cc. to a 500-lb. calf. Mercurial diuretics appear to be beneficial. However, various acidifying salts, such as 150 to 250 gr. potassium nitrate, twice daily, and ammonium chloride ½ ounce three times daily may be used, (4) blood transfusion, using citrated whole blood is particularly useful when an animal is anemic and weak.

Aureomycin in Calf Diseases

A report by C. Gaulier (*Rec. Med. Vet.*, March, 1953, through *J. Am. Vet. Med. Assoc.* 125:81, 1954) covers the clinical use of chlortetracycline (Aureomycin) in over 200 calves. The antibiotic was compared with penicillin, streptomycin, and sulfamerazine in a variety of calf diseases including infectious scours, septicemia, pneumonia, emphalophlebitis, peritonitis, and anthrax. Chlortetracycline proved to be the most effective of the four drugs. The author recommends 250 to 500 mg. orally three times daily for three to five days. The more seriously affected animals received 500 mg. intravenously twice daily.

It is Gaulier's opinion that, while in human medicine it has been reported that the simultaneous use of chlortetracycline and penicillin is sometimes incompatible, his experience has been to the contrary.

SRH for Canine Distemper

It is pointed out by C. A. Pleuger (*J. Am. Vet. Med. Assoc.* 125:111, 1954) that with the synthesis of sodium-sulfricin hydrazine (SRH), a new chemotherapeutic compound is available for the treatment of canine distemper. In his investigation of this preparation no signs of toxicity and no untoward side effects were observed following intravenous injections of SRH. This drug seems to neutralize toxins, reduce the severity of the disease, and hasten recovery. Since nearly all the cases were brought to a favorable conclusion without any negative reactions, it would seem probable that there is a neutralization of the toxic antigens and a stimulation of the defense mechanism of the systems which speeds up recovery.

On the basis of these observations, Pleuger concludes that intravenous injections of SRH are valuable in the treatment of canine distemper and that SRH is effective in the treatment of canine distemper and infectious bacteremias.

Trypsin in Veterinary Practice

D.F.M. Bunce (*N. Am. Vet.* 35:526, 1954) states that the proteolytic enzyme, trypsin, has been utilized in a wide range of diseases of animals characterized by the presence of a slough, purulent material and necrotic tissue. It was found to digest or liquefy purulent exudates, fibrin and blood clots, mucin and necrotic debris. No signs of sensitization or antigenicity in animals other than occasional transient hyperthermia are reported. It is a safe adjunct to any therapy, and treatment may be repeated at frequent intervals when necessary, without fear of side effects. Bacteria present in an infected lesion are rendered more susceptible to the action of antibiotics by the removal of their protective fibrinopurulent coating. Living cells are not affected by trypsin, due to the presence of certain antitryptic factors in viable tissue.

According to Bunce, good responses have been obtained in the trypsin treatment of pyometra, purulent sinusitis and foot rot of cattle. Small-animal practitioners are finding proteolytic enzymes to be of increasing value. Otitis externa, gravitational abscess following the insertion of an intramedullary pin, hematomata, suppurative arthritis, pyometra and cat abscesses respond readily to trypsin therapy, often obviating the necessity of surgical intervention and increasing the efficacy of adjunctive antibiotic therapy.

There are three modes of administration: (1) sprinkling or dusting the pure crystals on easily accessible surface lesions, (2) injection or infusion of a prepared solution into abscesses, sinuses or other closed cavities and (3) incorporation of the crystals into fast-melting gelatine capsules for insection into fistulous tracts or extremely heavy concentrations of purulent material. Adequate provision always must be made to permit suitable drainage of lysed material following enzyme therapy.

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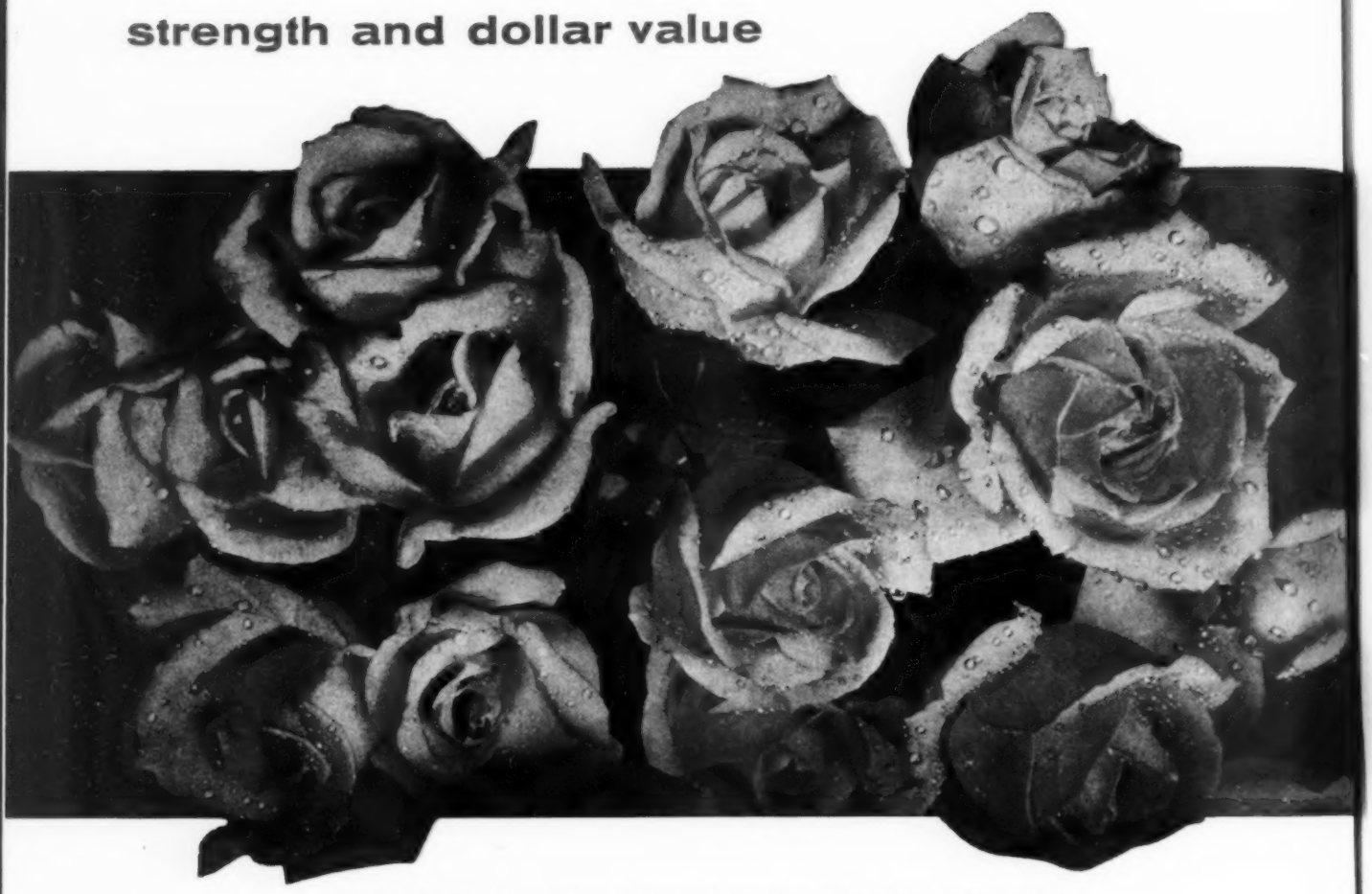

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Compounder's Corner

Paraldehyde Preparations

In the opinion of H. H. Hassler, G. Stabal and L. Cross (*Bull. Am. Soc. Hospital Pharm.* 11:124, 1954) paraldehyde probably comes closer to being an ideal hypnotic than any other drug available today. However, it still does not enjoy wide popularity in comparison with chloral hydrate and barbiturates. There are two factors which limit the usefulness of paraldehyde, taste and odor. Paraldehyde has a pungent odor end a burning disagreeable taste. The characteristic odor of paraldehyde appears on the breath within a few minutes after ingestion of the drug. In an effort to overcome the objectionable taste many formulas for paraldehyde preparations have been proposed. In reviewing these formulas it was found that none masked the objectionable odor and taste. In an effort to mask this taste Hassler and his associates attempted to emulsify paraldehyde.

Of the several formulas developed for making stable emulsions, the following was found to be by far the most palatable; having a very pleasant taste and leaving no after-taste:

Paraldehyde	**40.0 cc.**
Mineral oil	**44.0 cc.**
Polyoxyethylene sorbitan monostearate (Tween 60)	**5.0 Gm.**
Sorbitan monooleate (Span 80)	**5.0 Gm.**
Saccharin sodium	**0.3 Gm.**
Peppermint water, to make	**120.0 cc.**

Mix the mineral oil, paraldehyde, Tween and Span; then the saccharin is dissolved in the water. Slowly add the water to the oil mixture with constant stirring. This procedure is best accomplished using hand-stirring rather than a mechanical stirrer. Emulsions of paraldehyde made by hand-stirring are more stable than those made with mechanical mixers, there being less tendency for separation.

In response to requests for paraldehyde suppositories, H. Sheinaus and G. J. Sperandio (*Bull. Am. Soc. Hospital Pharm.* 11:52, 1954) developed the following procedure for providing the drug in this dosage form:

Polyethylene glycol (Carbowax) 6000	**25.0 Gm.**
Paraldehyde	**75.0 Gm.**

Melt the Carbowax 6000 in a suitable vessel over a water bath, and bring to about 70° C. Remove from bath, and add 15 cc. of paraldehyde, mixing thoroughly and rapidly until homogeneous. Add remainder of paraldehyde, mixing thoroughly and rapidly. Chill immediately to a temperature of approximately 35° C., and pour into suitable molds. Chill for 20 minutes before ejecting. The resulting suppositories are smooth, white, and lustrous. Seal immediately in cellophane and store in a cool place. Since paraldehyde is quite volatile, it is suggested that precautions be taken to minimize its loss by using a closed vessel during preparation. The mold size is left to the discretion of the compounder, depending on the dosage desired. Mold lubrication is unnecessary. The melting point of the product is 29° to 31° C.

These suppositories are non-toxic and non-irritating when given in proper dosage. They are rapidly-dissolving and constitute a ready and easily administered dosage form when oral administration is not deemed advisable.

Testing Shampoo Foam Power

A method for quickly checking the foaming power of shampoos has been developed by R. Colson (*Ind. de la Perf.* 2:53, 1954). In his method 40 cc. of shampoo solution are placed in the test apparatus and mechanically churned for one and one-half minutes. One cc. of a synthetic hair oil is then added, after taking the foam height, and the solution is again churned for one-half minute. The foam height is again measured, and the process repeated until 5 cc. of the synthetic soil have been added. The higher the first reading, and the closer the first and last readings, the better the foaming power of the shampoo. This simple test, which takes only ten minutes, can also be used as a check on the foaming power of detergents used in shampoo manufacture. The synthetic hair oil used in this test consists of:

Lanolin	**2.5 per cent**
Liquid petrolatum	**2.5 " "**
Dioxane	**95.0 " "**

Versatile Lotion Vehicles

Two versatile lotion vehicles to expedite the dispensing of dermatologic medicaments have been formulated by W. L. Schobel and J. L. Lichtin (*J.A. Ph.A.*, Pract. Ed. 15:420, 1954), as follows:

Lotion Vehicle A

Methylparaben	**0.25**
Propylparaben	**0.15**
Sodium lauryl sulfate	**10.00**
Propylene glycol	**120.00**
Stearyl alcohol	**25.00**
Light liquid petrolatum	**250.00**
Distilled water	**595.00**

Melt the stearyl alcohol on a water bath, add the liquid petrolatum, and heat to 70°. Dissolve the methyl and propyl parabens in hot water, add the sodium lauryl sulfate and the propylene glycol. Adjust the aqueous solution to 70°. Pour the mixture containing the water into the oil phase, in a fine stream, with continuous stirring. Continue to stir until the temperature is below 45°.

Lotion Vehicle B

Methylparaben	**0.25**
Propylparaben	**0.15**
Sorbitan monolaurate (Span 20)	**55.00**
Polyoxyethylene sorbitan monolaurate (Tween 20)	**25.00**
Sodium lauryl sulfate	**10.00**
Stearyl alcohol	**21.00**
Light liquid petrolatum	**400.00**
Distilled water	**500.00**

Melt the stearyl alcohol on a water bath, add the Span 20, light liquid petrolatum, and heat to 70° C. Dissolve the methyl and propyl parabens in hot water, add the Tween 20 and the sodium lauryl sulfate. Adjust the aqueous solution to 70°. Pour the mix-

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ture containing the water in a fine stream into the oleaginous mixture, stirring constantly. Continue to stir until the temperature is below 45°.

Both lotion vehicles *A* and *B* appear as bright white, stable, homogeneous, and cosmetically elegant emulsions. Lotion vehicle *B* remains on the surface of the skin longer than lotion *A* and appears to have greater emollient properties. On the other hand lotion *A* vanishes more readily into the skin. Both preparations were stable without creaming on the shelf at least two months at 20-30°. Upon refrigeration at 9°, the vehicles remained pourable after twenty-four hours. Exposure of the lotions to warm temperatures of about 33° did not affect them adversely. The *p*H of lotion vehicle *A* was 7.45, and *B* had a *p*H of 7.15. Tests have shown the formulas to be compatible with commonly prescribed medicaments.

Improved Calamine Lotion

Following a review of earlier work and extensive experimental studies of their own, J. Armstrong and A. H. Fenton (*Pharm. J.* 173:8, 1954) found that the undesirable thixotropic nature of the present calamine lotion of the British Pharmacopoeia can be obviated by the addition of sodium citrate. This modification yields an easily pourable fluid, while retaining the suspension form and dermatological advantages of the current official preparation. The improved formula is as follows:

Calamine	**150.0 Gm.**
Zinc oxide	**50.0 Gm.**
Bentonite	**30.0 Gm.**
Sodium citrate	**7.5 Gm.**
Glycerine	**50.0 cc.**
Phenol, liquefied	**5.0 cc.**
Water, distilled, to make	**1000.0 cc.**

Triturate the Malamine, zinc oxide, and bentonite with a solution of the sodium citrate in 700 cc. of water, add the phenol, the glycerine, and sufficient water to make 1000 cc.

Depilatory Cream

The production of a depilatory cream is described by G. Matsukara and his colleagues in Japanese patent 2,999 (through *Chem. Abstr.* 48:7855, 1954) as follows: A solution of 75 parts of 85 per cent strontium sulfide in 500 parts of water is heated for one hour on a steam bath, cooled to below 5° C., and filtered to obtain 450 parts of filtrate. The filtrate is heated with 40 parts of starch to obtain 400 parts of paste. This is mixed into 20 parts of 50 per cent sodium hydroxide and hydrophylic ointment to make 1,000 parts of finished product.

Evaluating Enteric Coatings

An *in vivo* method of testing enteric coatings for tablets and pills, based upon enzymic disintegration in the gastrointestinal tract of white rats has been devised by F. C. Hammerness and C. H. Waldon (*J.A.Ph.A.*, Scient. Ed. 43:351, 1954). In their procedure, pills containing a dye were given to a group of rats, and the time between ingestion and detection of the dye in the urine was noted. After a waiting period, enteric coated pills containing the dye were administered and the time between ingestion and detection of the dye in the urine again noted. If either the dye was not detected or the elapsed time was comparable to the blank, the coating was considered unsatisfactory. The coating was considered satisfactory if dye was noted after a reasonably increased lapsed time. The coatings used were cellulose acetate hydrogen phthalate and cellulose acetate stearate.

The investigators point out that this method of testing enteric coatings is based on natural action in the gastrointestinal tract of the white rat. The method is easily performed *in vivo*. The method gives satisfactory results and can be employed as a quick means of eliminating unsatisfactory coatings in experimental work in the development of new enteric coatings.

PVP in Aerosol Hair Lacquers

It is noted in *Schimmel Briefs* (No. 233, Aug. 1954) that some of the improved aerosol hair lacquers recently appearing on the market contain polyvinylpyrrolidone, briefly known as PVP. Aerosol lacquers based on PVP form a transparent film which adheres tenaciously to the hair but is water-soluble so it can be washed off easily. The film acts as a wave-set for resetting the hair when moistened with a wet comb. Unlike shellac, PVP takes up moisture from the air. If the humidity is not too high, this property is beneficial as the moisture acts as a plasticizer for the film. At high humidities the film becomes somewhat tacky. The addition of shellac to a PVP lacquer in the proportion of about 10 per cent of the weight of the PVP prevents tackiness. However, the presence of the shellac impairs the clarity of the film to some extent under conditions of high humidity. In a dry climate the film of unmodified PVP might be too brittle. In that case it is advisable to add a softening agent such as glycerine or dimethyl phthalate to the lacquer.

An aerosol hair lacquer based on PVP might be formulated along the lines indicated below:

Polyvinylpyrrolidone	**2.0 parts**
Shellac	**0.2 part**
Absolute alcohol	**17.5 parts**
Perfume	**0.3 part**
Propellent	**80.0 parts**

(selected to give a pressure of 35 lb. sq. in.)

Dental Anesthetic Ointment

According to the British Dental Journal (97:95, 1954, through *Pharm. J.* 173: 158, 1954) the following ointment, when applied to the gums before the injection of the anesthetic was found in 500 patients to eliminate the prick of the needle:

Xylocaine	**5.000 per cent**
Hyaluronidase	**0.015 " "**
Water-miscible base, to make	**100.000 " "**

Antimolding Agents in Syrups

The potentiating effect of antimolding agents in syrups was reported by O. M. Littlejohn and W. J. Husa in a paper presented at the 101st meeting of the American Pharmaceutical Association in Boston. Storage tests indicated that the concentration of the preservatives which had been found to prevent growth in Petri dish tests was not sufficient to prevent growth of molds under four different storage conditions in Simple Syrup, U.S.P., or diluted simple syrup (42.5 per cent sucrose w/v). Tests showed that there was a definite potentiating action among the parabens, but that the increase was not very great. There was only a slight potentiating action between benzoic and cinnamic acids, but when citric acid was added there was a large potentiating effect. Storage tests using mixtures of preservatives showed that for Syrup, U.S.P., a mixture of 50 per cent butylparaben and 50 per cent methylparaben at 1:4500 was the best for the inhibition of molds. In diluted simple syrup (42.5 per cent sucrose w/v) the use of either butylparaben 65 per cent and propylparaben 35 per cent at 1:7500, or butylparaben 90 per cent and propylparaben 10 per cent at 1:8000 was effective.

GLASS AEROSOLS FOR PHARMACEUTICALS

(*Continued from page 627*)

p.s.i.g. at 130° F. A solution of 90 per cent ethanol, for example, containing 25 per cent by volume of dichlorotetrafluoroethane, produces slightly lower gauge pressures at room temperature. As the temperature increases, the pressure of the alcohol-propellent mixture increases at a more gradual rate than that of the propellent alone. This is due to the increase in *miscibility potential*[2] of the alcohol mixture at the higher temperature, with such mixture acting as a diluent for the propellent. The use of such extraordinarily low pressures, 11 to 15 p.s.i.g. as, for example, compared to approximately 45 to 60 p.s.i.g. for carbonated beverages at room temperatures, makes it practical to utilize unprotected glass containers of suitable shape, structure and size.

5) *Cooling effect.* There is minimal cooling effect in products designed for topical application. One of the distinct disadvantages in using lower boiling point propellents is an unpleasant super-cooling effect on the skin. This should be avoided, particularly with products that might be applied to abraded or inflamed tissue.

Glass Specifications

While the variety of suitable container shapes is almost limitless, the design should avoid sharp corners and broad flat surfaces. The glass bottle should be constructed so as to allow a relatively uniform distribution of glass during the molding process with minimum wall thickness of 3 to 4 mm.

Figure 5 (see page 627) illustrates several two- and four- ounce bottle shapes currently available.

Until future technological advances in the glass industry make it practical, it is recommended that the unprotected glass containers should not exceed a volume of four ounces. Should economic or marketing considerations warrant the use of sizes larger than four ounces of current types, then suitable protective covering, e.g., fiberboard can or plastic coating, may be used. Such protection is also advisable for smaller sizes that are inherently weak in design, and of course, when individual preference dictates an additional "safety" assurance. Bottles containing pressures higher than those produced by dichlorotetrafluoroethane should have some kind of protective envelope.

Safety Considerations

In evaluating the relative safety of a product, or development, due consideration must be given to the normal intended use. For example, if an individual attempted to examine the level of fuel in his automobile tank with a lighted match, he would come to the conclusion that gasoline is a dangerous and unsafe thing. However, few, if any, of us express the slightest apprehension regarding the safety of gasoline under conditions of *normal* use.

Another example is the "pop" bottle. Literally billions of bottles of carbonated beverages are sold each year, and although their pressures at room temperature approximate 45 to 60 p.s.i.g., there is generally no apprehension involved in having such bottles in practically every home.

In setting up a test procedure to determine the safety of glass bottles used in the Ultra-Low Pressure System, due consideration must be given to the height from which such bottles normally would be dropped inadvertently. A standard drop test procedure has been developed whereby the aerosol bottles are first filled with alcohol base and propellent. Half of the bottles are then sprayed to one-third of the total volume. This is done to more nearly approximate conditions of use.

Half of each group of full and 1/3 full units are brought to temperature equilibrium at 70° and at 130° F.

The bottles are then dropped repeatedly from a standardized height of four feet onto a smooth surfaced concrete floor by means of a special dropping device (which in our laboratories we affectionately refer to as the Guillotine). (Figs. 6 & 7) This device insures that the test bottles are dropped under exactly the same conditions as the control beverage bottles. The number of drops required to break each bottle is then recorded. Details of the procedure and statistical analyses of the results are being published.

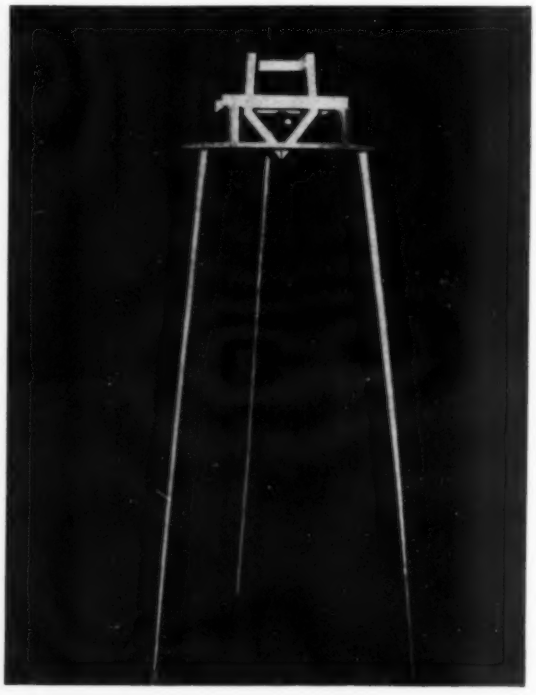
The height of four feet was chosen for two reasons:

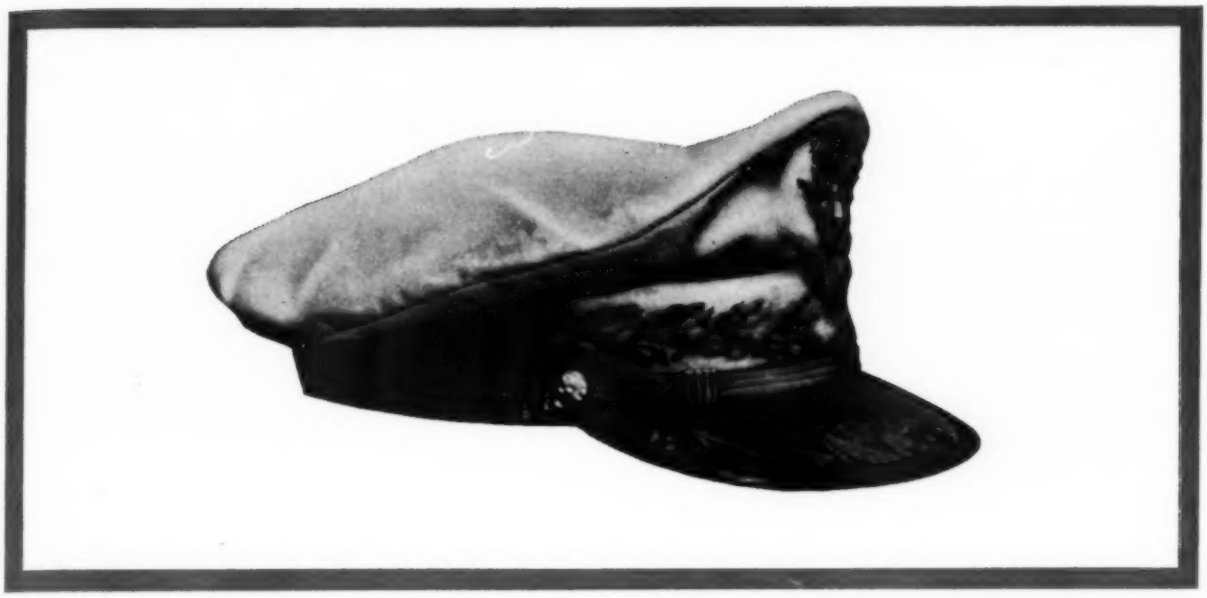
1) It represents the normal height from which bottles would be expected to drop accidentally, under normal usage.

2) It represents the minimum height, under the

(*Continued on page 684*)

Fig. 6





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(Continued from page 682)

described test conditions, from which 100 per cent of the beverage control bottles broke on the first drop.

Hurling such units from a height of say 25 feet, would show only that the bottle shatters violently when it breaks under such exaggerated conditions. Under such conditions, beverage bottles, and for that matter, non-pressurized bottles containing medicinals or any liquids, and even empty glass bottles and tumblers, would tend to shatter violently.

Based on the results obtained during extensive drop tests, the Ultra-Low Pressure System for pressurized alcohol-base products made its debut in its now familiar constricted waist two ounce bottle in October, 1953. Within the comparatively short time that has elapsed, well over one million units have been marketed in unprotected glass containers with several bottle shapes, and with no untoward effects. Certainly, this indicates successful packaging and merchandising. Several representative products are shown in Figure 8.

Products utilizing the three-phase principle, and the alcohol-base Ultra-Low Pressure System, available on the market are at present of the household items and cosmetic types. An ever-increasing number of product possibilities utilizing this system are being shelf-tested. Many pharmaceutical and veterinary products are well suited to these systems. Some examples of products under test are: antiseptic soaps, antiseptic solutions, burn remedies, local anesthetics, etc.

Summary

The convenience of dispensing, lack of corrosion, the gentleness of application particularly to sensitive tissue,

Fig. 7

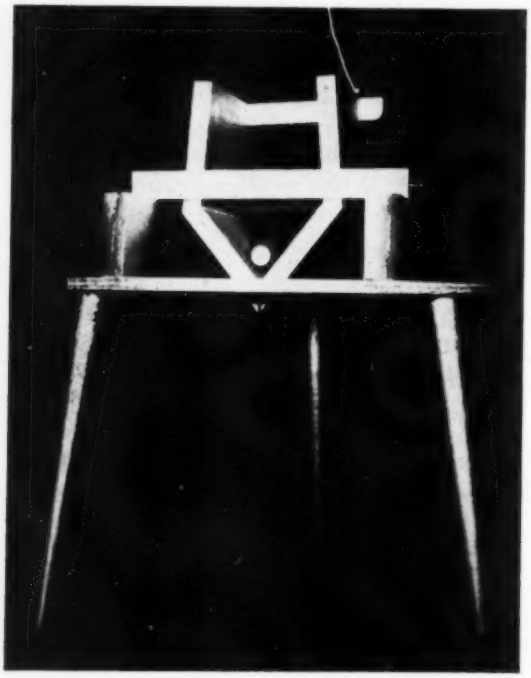


Fig. 8

and the minimization of product breakdown due to the exclusion of oxygen, and up to the great potentialties for the pharmaceutical industry in utilizing the glass aerosol.

REFERENCES

1. "The First Glass Aerosol," Modern Packaging, January, 1953.
2. "Dispensing Products by Internally Produced Ultra-Low Pressur Francis A. Mina, *Proceedings*, 40th Annual Meeting, C.S.M.A., December 1953.

ZINC BACITRACIN IN PHARMACEUTICAL PREPARATIONS

(Continued from page 613)

found to be non-irritating to the hair-free skin of rabbits. A clinical study on humans indicated no primary irritations or allergenic sensitizations from a petrolatum base ointment of the same potency.

Chemotherapy

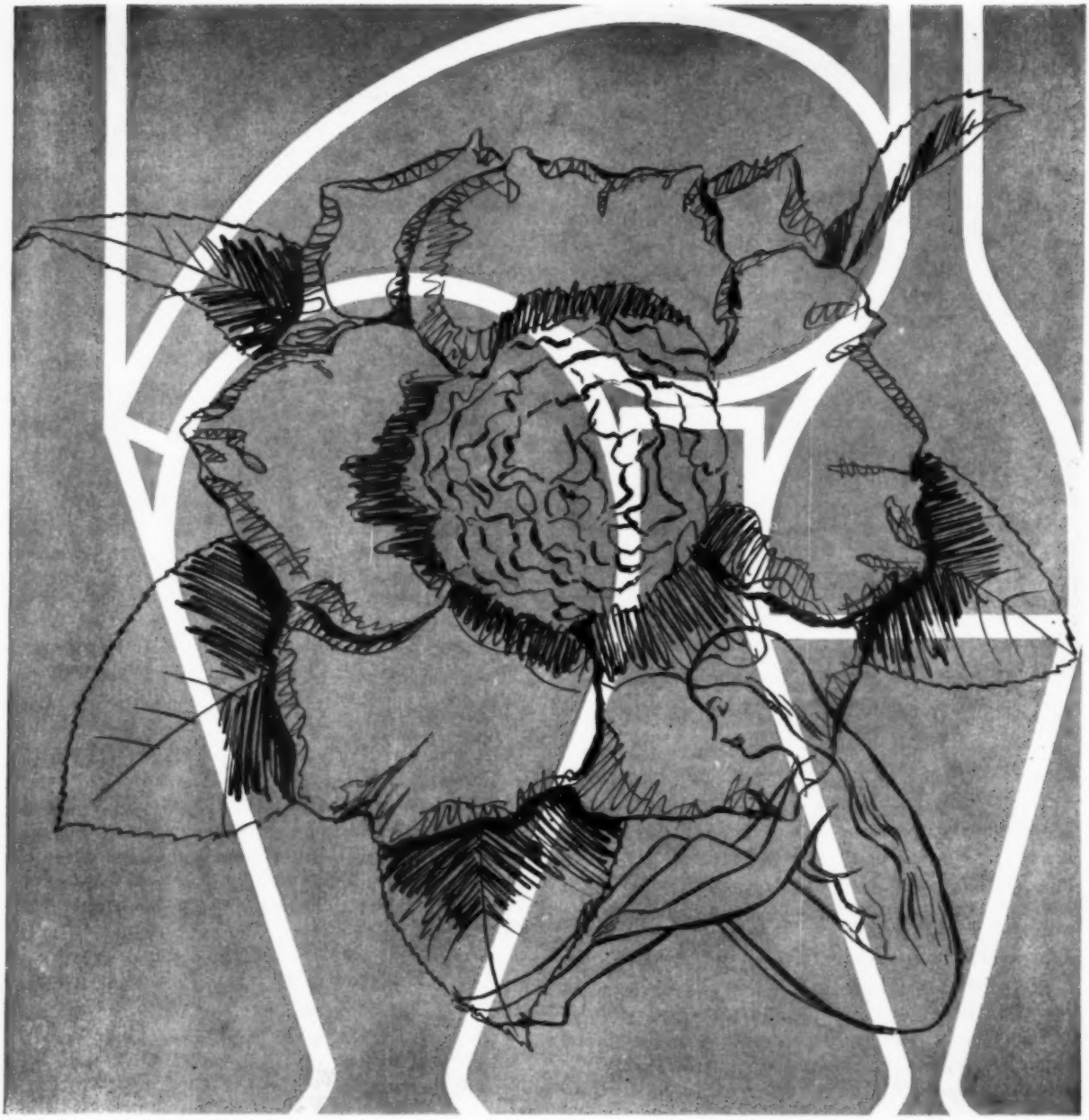
A comparative *in vitro* antibacterial activity study was performed on bacitracin and zinc bacitracin. Results indicated some differences in the relative effectiveness between bacitracin and the zinc salt, although the differences were of improbable significance. The test organisms used were *Gaffkya tetragena*, *Micrococcus flavus*, *Micrococcus pyogenes*, var. *aureus*, *Streplococcus hemloyticus*, *Escherichia coli* and *Bacillus mycoides*. An agar dilution-streak plate method was designed to check the possible antibiotic activity of the zinc ion. Tests indicated no antibiotic activity *in vitro* due to zinc ion present in zinc bacitracin and no depression of activity of bacitracin due to the presence of the zinc ion.

Troche formulations containing bacitracin and zinc bacitracin were evaluated for the availability of bacitracin activity in tests of bacitracin saliva levels. Results of the tests indicated no significant difference in saliva levels between bacitracin and zinc bacitracin troches.

Formulatory Compatibilities

Some compatibilities and incompatibilities may be of interest in new product formulation. Aqueous, alcoholic, and acetone suspensions exhibit losses in activity of varied degree relative to time and temperature of exposure. However, the use of these solvents is ap-

(Continued on page 686)



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(*Continued from page 684*)

plicable in the preparation of tablet granulations. Suspensions indicating some degree of stability may be prepared in vehicles of sesame or peanut oil with aluminum monostearate which have been preheated to drive off any moisture. Tests indicate that zinc bacitracin may be gas sterilized without significant loss in activity by tumbling in an atmosphere of 10 per cent ethylene oxide-90 per cent carbon dioxide.

There are indications that zinc bacitracin may be incompatible with quaternary ammonium compounds as demonstrated by benzalkonium chloride and cetylpyridinium chloride. It has been accepted that bacitracin is incompatible with methyl and propyl *p*-hydroxy benzoates, but zinc bacitracin has exhibited a greater compatibility. In a one-week test at 60° C. bacitracin lost 13 per cent potency but in the presence of parabens in utilizable concentrations it lost 84 per cent of its activity. Zinc bacitracin indicated insignificant loss but a 23 per cent loss when mixed with the same concentrations of parabens.

Other substances indicating favorable degrees of compatibility in useful concentrations are: mannitol, lactose, beta lactose, sucrose, gelatin, sodium chloride, magnesium stearate, calcium stearate, petrolatum, liquid petrolatum, benzocaine, cyclomethycaine, neomycin sulfate, polymyxin β-sulfate, *l*-ephenamine penicillin, streptomycin sulfate, saccharin sodium, polyoxyethylene sorbitan monolaurate and polyethylene glycol 400 dilaurate and distearate.

Assay

The microbiological assay for bacitracin is easily adapted to the bacitracin activity determination of zinc bacitracin by acidification of the aqueous extraction media with dilute hydrochloric acid to release the bacitracin from its insoluble salt.

Zinc Bacitracin Products

The synergistic antibiotic qualities[1] of bacitracin and neomycin have been exploited in the preparation of tablets for oral administration, ointments for topical application, and troches for buccal treatment. The substitution of zinc bacitracin for bacitracin in these preparations of the synergistic combination has resulted in products of greater stability.

Tablets containing 2500 units of bacitracin activity and 25 mg. of neomycin base as the sulfate were prepared with bacitracin or zinc bacitracin and subjected to a stability study at various temperatures.

THERMAL STABILITY OF BACITRACIN-NEOMYCIN AND ZINC BACITRACIN-NEOMYCIN TABLETS

Stored 3 months at	Percentage Retained Antibiotic Activity					
	60° C.		40° C.		25° C.	
	Neomycin Assay	Bacitracin Assay	Neomycin Assay	Bacitracin Assay	Neomycin Assay	Bacitracin Assay
Tablets Bacitracin-Neomycin	98	67	92	75	100	100
Tablets Zinc Bacitracin-Neomycin	100	90	100	96	100	100

Petrolatum base ointments containing 500 units of bacitracin activity derived from bacitracin or zinc bacitracin and 3.5 mg. of neomycin base as the sulfate per gram of ointment were prepared and subjected to a stability study at various temperatures.

THERMAL STABILITY OF BACITRACIN-NEOMYCIN AND ZINC BACITRACIN-NEOMYCIN OINTMENTS

Stored 6 months at	Percentage Retained Antibiotic Activity					
	5° C.		25° C.		40° C.	
	Neomycin Assay	Bacitracin Assay	Neomycin Assay	Bacit.acin Assay	Neomycin Assay	Bacitracin Assay
Ointment Bacitracin-Neomycin	100	100	100	92	99	70
Ointment Zinc Bacitracin-Neomycin	100	100	100	95	95	90

Many clinicians favor a water-miscible or water-soluble ointment base as the vehicle for topical antibiotics. Bacitracin has been used in such a base by Meleney[2], but suffers a rapid loss in activity at room temperature. This is typical of bacitracin in bases containing glycerols, glycols, alcohols or water. Zinc bacitracin prepared in the 55 per cent propylene glycol-45 per cent Carbowax 4000 ointment base experienced a 15 per cent loss in activity when stored at room temperature for one week as compared to the 45 per cent loss suffered by bacitracin. The comparative study of bacitracin and zinc bacitracin in the Meleny base indicated the greater stability of zinc bacitracin but also indicated that it had similar incompatibilities with glycerols, glycols, alcohols or water.

Investigation has been carried out on two types of troches containing bacitracin. One type of commercially available troche is prepared on a tablet machine using a hard tablet granulation and setting the tablet machine pressure to result in a tablet of great hardness and little ability to disintegrate. Another type troche is that made by a fusion process which results in a hard-candy troche. The antibiotic is added to a molten candy mass, distributed and place in a device which forms the unit dosage form.

A study of the tablet-machine compressed troche utilizing bacitracin and zinc bacitracin indicated the zinc salt lended greater stability to the product. A troche claiming 1000 units of bacitracin activity prepared with a 25 per cent excess has been found to experience a drop in potency to 85 per cent of label claim in a period of 18 to 24 months. The same formulation containing zinc bacitracin of the same labeled potency prepared with a 10 per cent excess of zinc bacitracin exhibited a one per cent loss in activity from label claim in 18 months and about six per cent loss in 24 months.

The preparation of the candy type troche exposes the antibiotic to heat for a considerable time period. The candy troche manufacturer suggests an antibiotic level of preparation for bacitracin utilizing 200 per cent of label claim. A 45 per cent loss in total input activity was experienced during production. Several similar formula batches of zinc bacitracin troches have been

(*Continued on page 692*)

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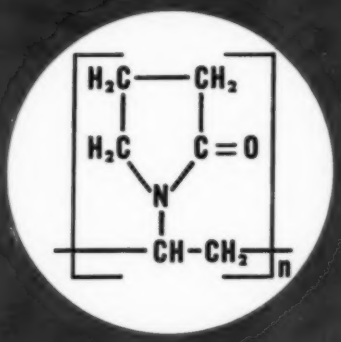

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Perfumer's Shelf

Oil of Erythroxylon Monogynum Wood

The essential oil from the wood of *Erythroxylon monogynum* has been investigated by R. C. Gupta and M. S. Muthana (*J. Indian Inst. Sci.* 36A:76, 1954). The wood was steam distilled and a greenish oil was obtained in 16.6 per cent yield from the Royalaput variety and 0.085 per cent yield from a Magalo sample. The oil had the following properties:

Specific gravity	**0.9333**
Index of refraction	**1.494**
Specific rotation	**+18.9**
Acid value	**6.6**
Ester value	**10.79**
Acetyl value	**60.17**

The oil was fractionated into five fractions. Fraction 1, consisting of 40 per cent of the oil, was alpha-pinene. Fractions 2 and 3, consisting of sesquiterpenes, were so small in quantity that they could not be purified and were not identified. Fraction 4, consisting of 50 per cent of the oil, was a diterpene, the constitution of which is not known. Fraction 5, consisting of 1.8 per cent of the oil, yielded a crystalline white solid that was identified as a diterpene alcohol whose constitution is unknown.

Formosan Oil of Ocimum Gratissimum

Jun-Cheih Wang (*Formosan Sci.* 2:62, 1948 through *Chem. Abstr.* 48:7853, 1954) reports that the essential oil from *Ocimum gratissimum*, obtained in 0.5 per cent yield based on the dried Formosan plant, had the following properties:

Specific gravity	**0.9920**
Index of refraction	**1.5150**
Specific rotation	**–12.4°**

Chemical analysis of the oil showed that it contains a trace of cadinol, 60.5 per cent of eugenol, 19.4 per cent of ocimene, and 10.0 per cent of cadinene.

In Wang's procedure for the selenium dioxide oxidation of cadinene 83.8 Gm. of cadinene in 500 cc. of ethyl alcohol is heated with 46 Gm. of selenium dioxide (in alcohol) for nine hours at 80 to 87° C. The color of the reaction mixture changes from yellow to brown, to red, and finally to black. The selenium precipitate is filtered and the solvent is evaporated. The residue, on distillation, gives an oil boiling at 230° C. and with a specific gravity of 0.9497 and an index of refraction of 1,5369. An attempt to prepare a semicarbazone of this oil failed. It is apparently a dimer of cadinene.

Bulgarian Rose Oil

Rose oil, says J. F. Stirling (*Perf. & Essent. Oil Rec.* 45:52, 1954) is still one of Bulgaria's principal exports to Western Europe. The oil is obtained from two rose varieties, *Rosa damascena* and *Rosa alba*, both rich in essential oils. The extraction of one kilogram of rose oil requires three to four thousand kilograms of petals—about two million roses. The oil is extracted from the petals by water distillation. The majority of the stills used are the direct-fire type, but there are also a few steam-heated stills.

The first distillation produces about .001 per cent of the greenish oil, which is "spooned off" from the top of the distillate, after standing for some time in Florentine flasks. The residue, known as the "First Water," is redistilled with fresh rose petals. The second distillation produces about 45 grams of "water oil" for every thousand liters of the accumulated First Waters. From the distilleries, the oil goes to State-owned laboratories, where it is analyzed. Only completely pure rose oil is released for export, and is shipped in special containers, called Konkumi. These have a tin lining, and are protected by an outer casing of white cloth, which now displays the national emblem of Bulgaria. Being highly priced, the rose oil has often been subject to adulteration, usually by palmarosa, wood oil and spermaceti. But it is claimed that the strict control of standards, now imposed by the Government, makes it impossible for adulterated or inferior Bulgarian oils to be put on the world market.

Other Bulgarian rose products are rose water, rose concrete and rose absolute. The absolute is a brown, waxy substance, partly soluble in alcohol. It is extracted from the petals by volatile solvents. Rose absolute is a thick greenish-brown liquid, soluble in alcohol. These products are used in the manufacture of perfume, liqueurs and confectionery.

Eau de Cologne

It has been recommended, says T. Ruemele (*Perf. & Essent. Oil Rec.* 45:53, 1954) that the less complicated the composition of the Eau de Cologne the more pleasant, delicate and harmonious the emanating fragrance. Nonetheless, an appreciable deviation from the basic classical and simple bergamot-citrus-neroli complex has taken place, as a result of which quite an ample number of variations were produced. There appear to be three ways in which the orthodox mixtures can be modified. These include: (1) Incorporation of new components, obviously compatible with those already present; (2) Substitution of one or all the components for suitable alternatives; and, (3) Olfactory predominance of one of the constituents of the mixture.

The incorporation of new components is entirely of French origin, and the recommendations deriving from those sources involved the blending of the classical specification with lavender oil, orange oil and rosmarin oil.

Apart from the obvious exchange of the components of natural origin for the corresponding synthetic products, it has been advised that compounds such as bergamot oil, neroli oil, lavender (or rosmarin) oil and lemon oil might preferably be substituted as follows: bergamot oil: cedrat oil, lime oil, mandarine oil, grape fruit oil; neroli oil: petitgrain oil; lavender (or rosmarin) oil: thyme oil, oil of sage; lemon oil: vervain oil, helm mint oil.

According to the olfactory predominance of one of the major constituents

TOP NOTES by

FLOWER of the Month

October — Calendula
or Cosmos

November — Chrysanthemum

MAYBE YOU KNOW HIM . . .

ARMED with unquenchable ambition and a B.S. in biochemistry, GEORGE SCHMIDT said farewell to his alma mater, the University of Maine, in the summer of 1940 and came to New York seeking fame and fortune. He was well on his way to acquiring both when Uncle Sam and the U. S. Army decided in 1942 that they, too, needed him. Four years later, after active service in England, France, Belgium and Germany, Major Schmidt returned to private life. As food chemist for his firm, a leading manufacturer, where quality and uniformity of raw materials and finished goods were the only criteria of acceptability, George had his first introduction to Fritzsche products. It was on the strength of this acquaintance, after several years devoted to production, purchasing and research, that he sought his present connection with Fritzsche Brothers. He wanted to apply his knowledge and abilities to the field of sales and he attributes much of his success in converting difficult prospects into ardent users of our merchandise to the confidence that was born of his practical experience with many of the materials he now sells. George's territory embraces parts of New York State and Northern New Jersey, where he will soon reside. When not energetically promoting Fritzsche products, his interests revolve around a lovely family—his wife, daughter and two sons, —his home and garden, coin collecting and outdoor sports.

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three main groups can be ascertained, namely, the fruity, the floral, and the fancy group. In the first section the fruity note is produced either by the neroli oil or by the lemon oil or the bergamot oil, the latter being frequently quite distinctly pronounced in character. As a result of the inclusion of floral ingredients, such as lavender oil, rose oil, violet oil, lilac oil or geranium oil, the second group is formed. Finally, the third group is generally initiated by bouquetting appropriately the floral components.

After stressing the importance of alcohol as a solvent in making Eau de Cologne, Ruemele points out that the aging period is another important factor governing the quality of these products. This is the period during which, due to chemical reactions, the latent state of the odor progresses towards stability and efficacy. It should be remembered that aging does not improve essences characterized by a low quality from the beginning. The period of aging should be as long as three months, at a suitable temperature, say ±10° C. The product must be kept in well-closed containers, preferably filled entirely, in a dark place. This procedure will activate the aging and prevent considerably the oxidation. There are artificial methods (*e.g.* ultrasonics) which would decrease appreciably the period of aging, but it cannot yet be said whether such a method is equivalent to the orthodox procedure. The incorporation of substances, such as various acetates, with a view to simply providing an illusion that aging has taken place, must be classified as a method deliberately detrimental to the fragrance conferring to it a peculiarly odd top note. It is apparent that only a true aging will contribute materially to the successful formation of the charming and striking scent which is required in such a popular product.

Autoxidation of Alpha-Pinene

In a paper presented before the Division of Organic Chemistry during the 126th meeting of the American Chemical Society in New York City, R. N. Moore, C. Golumbic and S. S. Fisher pointed out that although the autoxidation of α-pinene has been studied intermittently for over 100 years, few data are available on the products obtained by non-catalytic, liquid-phase autoxidation at elevated temperatures. In the present investigation, α-pinene was autoxidized in the dark at 100° C. and the α-pinene hydroperoxides in the resulting oxidate were reduced. The product was fractionated by careful distillation at reduced pressure, and the volatile fractions were analyzed by chemical and physical methods, including infrared and ultraviolet absorption measurements.

In addition to unreacted α-pinene (45 per cent of the volatile material) and verbenone (nine per cent), verbenol (16 per cent), and verbenene (trace) which have long been recognized as products of the reaction, α-pinene epoxide (13 per cent) and transpinocarveol (eight per cent) were obtained. It is pointed out that G. O. Schenck and his associates have recently reported the identification of this epoxide among the products obtained by low temperature autoxidation of α-pinene. Pinocarveol has not been previously identified as a product of the nonphotosensitized autoxidation of α-pinene. It is suggested that this product results from free radical attack on the 1-methyl group of α-pinene to give a myrtenyl free radical which resonates to the pinocarvyl free radical and yields pinocarvyl hydroperoxide.

Prolonged Menthol Inhalation

The effects of prolonged inhalation of menthol vapor on the intact animal, with special reference to the upper respiratory tract, has been studied by N. Rakieten, M. L. Rakieten and M. Bogkin (*J. Am. Pharm. Assoc.* Scient. Ed. 43:391, 1954). In their experiments, rats exposed to menthol in concentrations of 0.087 ± 0.021, 0.148 ± 0.031, and 0.259 ± 0.166 p. p. m. for 71, 74, 75, and 79 days shows no over-all gross toxic effects as evidenced by: (*a*) normal growth curves as compared with controls; (*b*) comparable food and water consumption as the controls; (*c*) comparable values of hemoglobin, red blood cells, white blood cells, and differential counts when compared with controls; (*d*) no increase in eosinophil counts; and (*e*) an infrequent conjunctivitis during exposure to menthol vapor which cleared soon after the exposure was completed.

Histopathological examination of tissues showed no significant changes in the nasopharynx, turbinates, heart, spleen, liver, kidney, eye, skin, ovaries, testes, skeletal muscle, and brain. Changes indicative of "irritation" were seen in the lungs of the animals exposed to the highest concentration of menthol. In the animals exposed to 0.087 and 0.148 p.p.m. of menthol, no greater changes were seen in the respiratory system than were seen in comparable control animals. Ciliary activity in fresh preparations of the tracheas of the animals exposed to all concentrations of menthol vapor was normal.

Product with Jasmine Odor

In Japanese patent 4070 (through *Chem. Abstr.* 48:9024, 1954), Y. Toyama presents the following method for producing a substance having a jasmine-like odor. Fatty acid, mainly 14-hydroxypalmitic acid, from beeswax is lactonized to obtain a product boiling at 150° C., with a specific gravity of 0.9369 and an index of refraction of 1.4690.

Malabar Lemon Grass Oil

Two samples of oil, known locally in India as Malabar lemon grass oil, obtained from a plant provisionally identified as *Cymbopogon nardus*, have been examined by K. K. Chakravarti and S. C. Bhatlacharyya (*Perf. & Essent. Oil Rec.* 45:184, 1954). They note that, apart from the name, the oil has very little similarity with lemongrass oil. It possesses a sweet persisting odor which should make it an excellent perfume for soap and other cosmetics. It shows the following properties:

Specific gravity	**0.9353**
Index of refraction	**1.4839**
Specific rotation	**27. 2**
Acid value	**1.12**
Ester value	**8.3**
Ester number, after acetylation	**110.8**
Carbonyl value hydroxylamine method)	**12.93**

Distillation data showed that the lower boiling fractions of Malabar lemongrass oil has roughly the following composition:

Constituent	*Quantity in per cent (based on the total oil)*
l-α-thujene	0.5
l-α-pinene	2.9
l-camphene	22.0
l-limonene	6.5
l-borneol	14.0
l-α-terpineol (?)	1.6
Residue, intermediate fraction loss etc.	4.8

The higher boiling fraction was found to contain sesquiterpene hydrocarbons, and alcohols and some diterpene derivatives as well. Some of these are azulene in nature. These will be described in a later paper.

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Abreast of the Markets

Tartrates Advance in Price

For the first time in about three years, tartaric acid as well as the tartrates went up last month anywhere from one to four cents a pound. Cream of tartar is now selling for 34 cents; Rochelle salt, 36 cents; tartar emetic, 67 cents; and tartaric acid, 42 cents a pound. Among the causes for this price change are a greater demand for the items, increased costs of the raw materials and a firmer market in tartrates in Europe.

Methionine Reduced

The price of pharmaceutical grade DL-methionine was reduced about 20 per cent last month, with the price of 50 pounds or more of the item now being $3.50 a pound.

Caffeine Is Brisk

Caffeine prices are on the firm side, with the alkaloid now selling for $3.15 a pound, and the citrated caffeine, for $2.90. While there are sufficient stocks to take care of the pharmaceutical needs at the present time, there are indications that the item will continue on the firm side. The United States is now importing very little material, if any at all, from Europe owing to the fact that most of the foreign production is being consumed by the local European markets.

Citral Higher

Reflecting the higher cost of lemongrass oil from which it is derived, citral advanced to $5.05 last month. It appears that this aromatic will continue to go higher, keeping in step with the essential oil.

Menthol Still Unsettled

The menthol picture was clouded last month by the inconsistent demand for the product. The price of the Brazilian material remained at $8.50 a pound for the present time; however, all signs point to a firming market in the new year, should demand pick up as it is expected to do.

Dealers indicate that this year's short Crop will force the prices up as soon as spot supplies are decreased and replacements become more difficult to obtain. Producers of the Brazilian menthol, it is said, have become disgruntled in recent years by the low prices they have been receiving and therefore cut down on their plantings.

Agar Price Reduced

In spite of the fact that the 1954 production of agar agar was below normal, the anticipated shortage has not developed. Quite the contrary, the price of the item fell off to $3 a pound last month, largely because of a very sluggish demand.

In some quarters, a firming is expected during the early part of next year, at which time the stocks on hand are expected to be depleted. It is too early yet to make any predictions.

Papain Steady

The spot price of papain has not changed in recent weeks, although the top grades have been advancing at the origin. The chief cause of this development is that sufficient low-quality stocks have been arriving on the spot market to keep the price down.

Vanilla Beans Unchanged

The vanilla bean spot market was rather uneventful last month, with both the local and foreign prices remaining on a firm level. Bourbon vanilla beans were being quoted at $10.50; Mexican cuts, at $10.25; and Mexican whole beans, at $10.50 a pound. Importers were of the opinion that the prices would continue to advance in the near future.

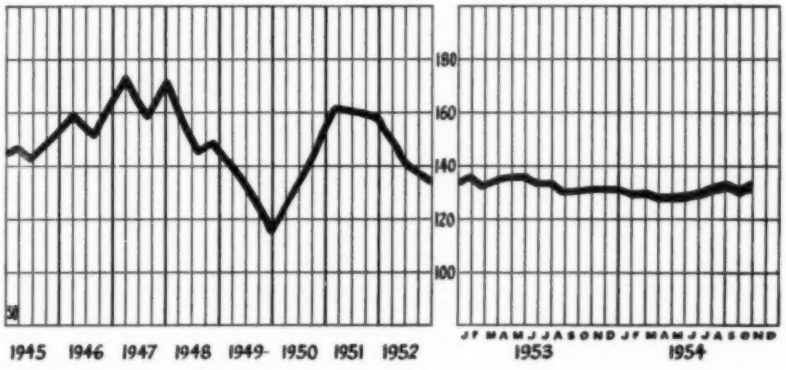
Lemongrass Oil Up

Lemongrass oil advanced steadily last month to the range between $2.50 and $3 a pound. The prospect of this oil is one of continued firmness owing to the general shortage of the material, both on the spot market and in the origin.

Peppermint Oil Jumps Ahead

The 1954 crop of peppermint oil was quite low in high-quality material, and this resulted in last month's abrupt price increase for both the natural and redistilled oil. The former is now selling from $7.75 to $8.50, and the latter, from $8.50 to $9 a pound. It appears that, although some lower prices are still being quoted, the high test oil will continue to advance in the months ahead.

50 RAW MATERIALS—WEIGHTED PRICE INDEX. 1926 - 100.



The price index of fifty commodities for October advanced from 126.6 to 130.9.

(*Continued from page 686*)

prepared using a 50 per cent excess of label claim bacitracin activity and the resulting product exhibited only a seven per cent loss in total input potency in production. This points to a means of reducing the percentage excess bacitracin necessary to produce this type of troche. Candy type troches containing zinc bacitracin have an acceptable taste with no detectable bacitracin bitterness. Candy type troches have been prepared as antibiotic combinations with *l*-ephenamine penicillin and neomycin sulfate and exhibit acceptable tastes and stabilities.

Zinc bacitracin has been formulated with various tooth powders to provide an antibiotic dental preparation. The tastelessness of the zinc salt in tooth powder mixtures was evidenced and no undesirable taste effects were detectable in the formulations. Studies indicate favorably stability for 50 unit per gram formulations at room temperature for one year. Fitzgerald and Jordan[3] of the National Institute of Dental Research, National Institutes of Health, have tested various antibiotics and found bacitracin to be specific for heterofermentative types of lactobacilli contributing to dental caries.

Summary

Zinc bacitracin exhibits a greater antibiotic stability than bacitracin. This salt of bacitracin is useful in oral and topical pharmaceutical preparations to provide bacitracin activity in a form which assures greater product stability, which affords greater facility in product manufacture and which offers a relatively tasteless oral antibiotic.

The author is indebted to Messrs. F. W. Chornock, J. N. Spencer and R. S. Baldwin of the Pharmaceutical Research Division, Commercial Solvents Corporation for chemical, pharmacologic and chemotherapeutic data;

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PATENT THOUGHTS and TRENDS

(*Continued from page 643*)

Exhibit 48, dated February 11, 1946, mentions tests on human beings, as well as the other requirements, for antiperspirant activity. It appears from a careful reading of the entire record that nobody actually carried out a detailed test to determine whether the material actually stopped or decreased markedly the perspiration of a human being (Requirement (c) above). It appears that more simple alternatives were attempted, such as the protein precipitation test . . . or the frog skin test. . . . The defendant's protein precipitation test was completed before the plaintiff's frog skin test. Even with the frog skin test, the defendant's samples seem to have been submitted earlier (June 12, 1946) than that of Andersen (probably June 15, 1946. . . . Neither party can successfully maintain that either of these tests is a quantitative measure of actual antiperspirant activity in human beings. . . . Each of these tests measures one of the properties (blocking of pores, contraction of skin) which contribute to actual antiperspirant activity.

First Commerical Products

The judge found that Arden had in fact put out a commercial product before Reheis but nevertheless felt that Reheis had worked out completely requirements (a) and (b) for the antiperspirant potentialities of aluminum chlorohydrate and carried out one very promising test, protein precipitation before Andersen had even heard of aluminum chlorohydrate. The judge felt that the essential difference between Reheis and Andersen was that Reheis did virtually all the work necessary to demonstrate the antiperspirant potentialities of aluminum chlorohydrate, but did not put the product on the market; whereas Andersen participated in only one phase of the preliminary testing, used Reheis' data on the other factors and marketed the material.

Further, the judge felt that there was no merit to the contention that the use of aluminum chlorohydrate with an emulsifier involved invention. The judge cited the action of the Patent Office which did not consider the process of preparing aluminum chlorohydrate in an emulsion form as an invention as such, but insisted that aluminum chlorohydrate be specified as the constituent.

Aside from public acceptance, the judge felt that Andersen did not anticipate Reheis in any particular. The judge stated his belief that the pH values listed in the patent were also secured from information supplied by Reheis.

Finally, even as to public distribution, the judge cited evidence that others anticipated Arden. In this connection the judge mentioned that the Puritan Company used aluminum chlorohydrate in batch manufacture, and that this was sold to Marian Bialac, a distributor. While the product was used in a solution without an emulsifier the court felt that this was of no significance.

A. Is the Use of Aluminum Chlorohydrate as an Antiperspirant an invention in view of the Prior Art?

B. Is the Combination of Aluminum Chlorohydrate with an Emulsifier an Invention?

The judge held that the Patent Office would not have considered the combination of an undefined basic aluminum chloride with an emulsifier as patentable. Rather it was the use of this particular aluminum chlorohydrate form of basic aluminum chloride in a

(*Continued on page 699*)

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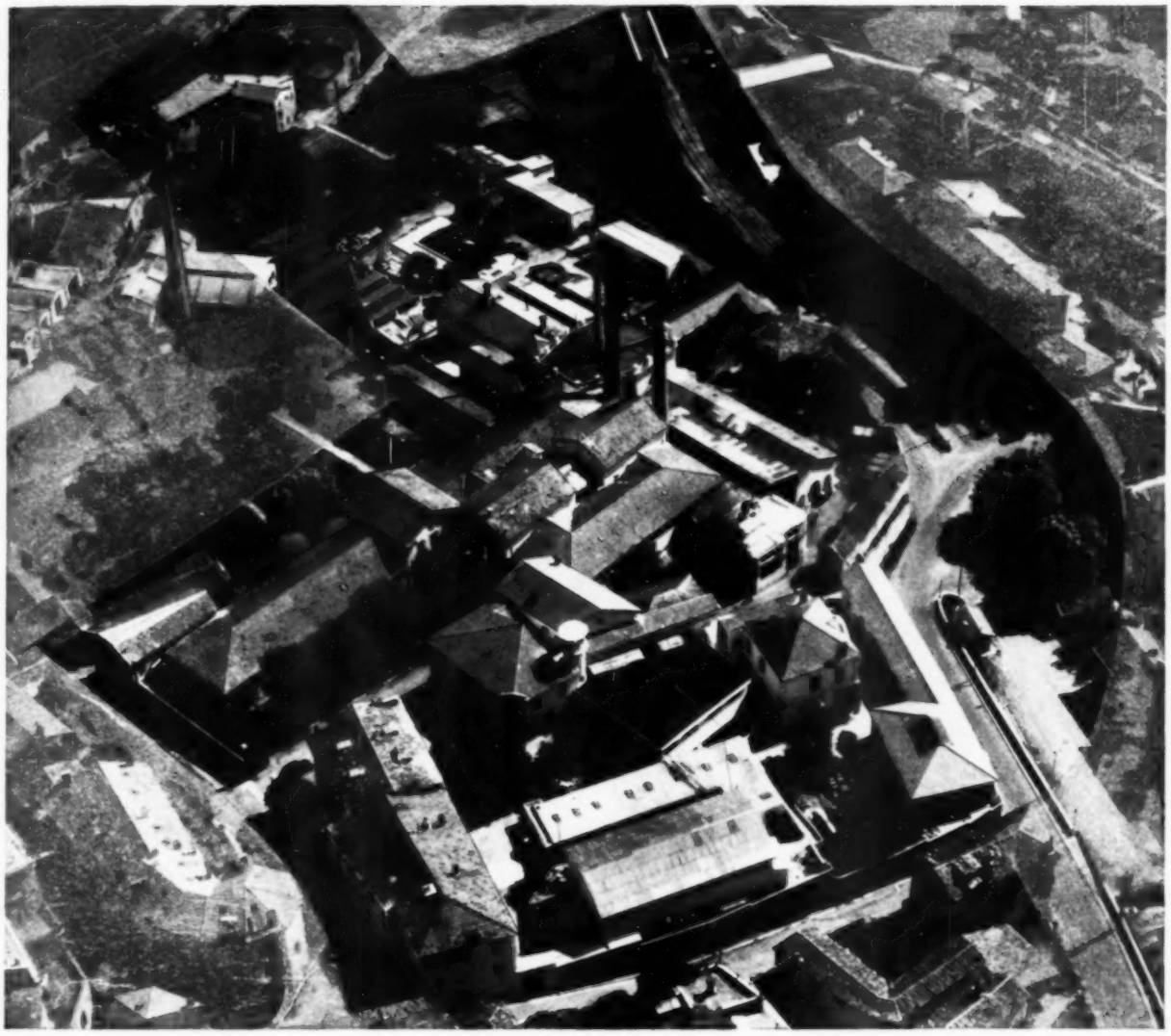

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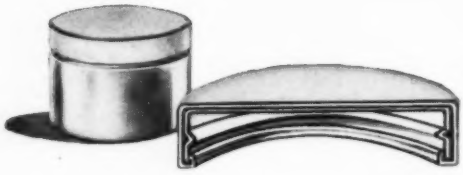

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Readers' Questions . . .

Cold Wave Neutralizers: *We take the liberty of inquiring whether it is possible for you to let us have a good formula for a neutralizer for cold permanent waves.* BRUSSELS.

Hydrogen peroxide with addition of an organic acid is suitable, as in the following example:

Solution hydrogen peroxide, six per cent	**50 cc.**
Tartaric acid	**3 Gm.**
Distilled water, to make	**100 cc.**

Many cold wave kits use solid neutralizers with directions for the preparation of the solution. The most widely used solid neutralizer is potassium bromate, packed in air-tight envelopes of cellophane or similar material; ¼ ounce to be dissolved in 16 ounces of warm water is adequate. As potassium bromate is poisonous if taken internally, appropriate warnings must be included in the directions.

Powdered Silk in Hand Lotions: *Can you give me a formula incorporating powdered silk or powdered satin as one of the ingredients for a liquid hand lotion?* WORCESTER.

I regret that I have no specific formulas on this particular application. However, considerable information on the use of silk in cosmetic preparations was described in an abstract appearing in the July, 1950, issue, page 101 of DRUG & COSMETIC INDUSTRY.

A British patent was also discussed in the May, 1949, issue, page 613. The September, 1953, issue, page 375, carries an abstract of a Japanese patent that describes the manufacture of powdered silk.

I have no information on the use of powdered satin in cosmetics nor have I seen references to such applications.

Marketing a Hand Cream: *I am interested in marketing a hand cream. Can you advise me on the necessary steps to be taken? I have my formula and also ideas for selling it, but from here on out, I'm stumped. Must I have a laboratory set-up to meet government regulations, must I be licensed, must the formula be submitted to the A.M.A. before it can be sold, etc., etc.? Thanking you in advance for your cooperation.* YONKERS.

You do not have to maintain a laboratory or manufacturing plant in order to sell a cosmetic. This can be done for you by a private label house and all you would be concerned with would be the distribution

and selling of the product. Unless your hand cream contains some unusual material or unless you make therapeutic claims for your product, there is no need to submit your formula to the Food & Drug Administration. The American Medical Association has nothing to do with passing on the merits or demerits of your product. It is my suggestion that you contact one of the private label houses or consultants listed in the advertising pages of our publication.

Dandruff Lotion: *I am interested in obtaining a formula for a dandruff lotion. I should like something that is fairly simple to prepare and containing standard ingredients.* NEW YORK.

Many so-called dandruff lotions are made with resorcinol as the active ingredient. Typical is a lotion containing:

Resorcinol	6.0 parts
Glycerine	10.0 "
Alcohol	9.6 "
Water, to make	100.0 "

It should be noted that while resorcinol has no appreciable effect on dark hair, it is apt to discolor blond, grey or white hair. Resorcinol monoacetate, which is less likely to stain the hair, is often used in its place in equal amounts.

Quaternary ammonium compounds are also finding use in the preparation of such hair and scalp lotions. The concentration to be used will vary somewhat according to the type of quaternary compound employed.

After-Shave Cream Lotion for Electric Razors: *Please send me a formula for an after-shave lotion to be used following shaving with an electric razor. I prefer something that is soothing and emollient rather than stimulating.* LOS ANGELES.

I think that a liquid cream made along the following lines will meet your requirements:

Glyceryl monostearate (self emulsifying)	3.5 parts
White oleic acid	2.0 "
Glycerine	5.0 "
Triethanolamine	0.8 "
Menthol	0.1 "
Water	81.6 "
Alcohol	7.0 "
Perfume	sufficient
Preservative	"

Melt the glyceryl monostearate with the oleic acid. Heat together the glycerine, triethanolamine, preservative and water to approximately the same temperature and add to the first mixture with high speed stirring. When the temperature drops to 50°, add the menthol and perfume dissolved in alcohol. Continue stirring until the emulsion is cool.

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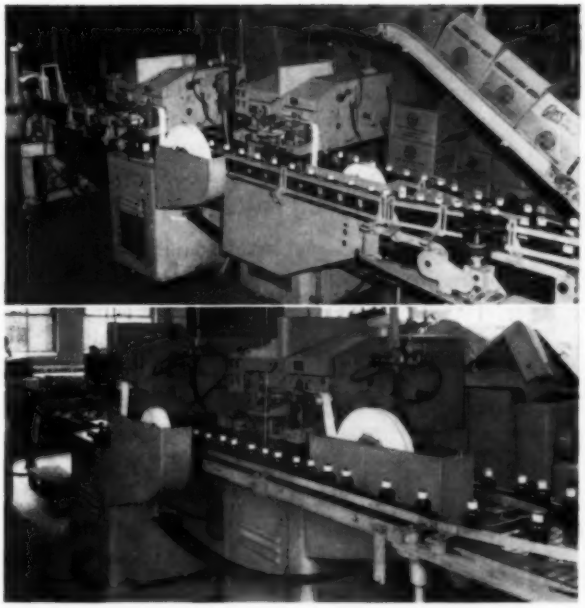

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Industry's Books...

The Effect of ACTH and Cortisone Upon Infection and Resistance, *Edited by Gregory Shwartzman, M.D., Symposium Held at the New York Academy of Medicine March 27 and 28, 1952, 204 pp., Illus., Columbia University Press, New York, (1953), Cloth,* **$5.50.** Here is an important contribution to the growing body of medical knowledge that has given new direction to the study of infection and resistance. In this symposium thirty-one authorities discuss many phases of the effect of ACTH and cortisone on infection and resistance. Effects of the hormones on metabolic functions and structural elements are also considered in the hope that knowledge of these basic facts will aid an understanding of the mechanism of the effect of hormones on infection and resistance.

General Chemistry, *A Topical Introduction, by Eugene G. Rochow and M. Kent Wilson, Department of Chemistry, Harvard University, 602 pp., Illus., John Wiley & Sons, Inc., New York, (1954), Cloth,* **$6.** This book has been written to provide the freshman college student with a sound introduction to selected topics in general chemistry. Designed to cover portions of the field rather than its whole, the book relates chemical fundamentals to the present-day experience of students. It treats these principles as thoroughly as freshman preparation in mathematics and general science will permit. The result is a simplified approach to the subject, shorter and more readable than most texts.

The Megaloblastic Anemias, *by L. J. Davis, M.D., Muirhead Professor of Medicine in the University of Glasgow, and Alexander Brown, M.D., Senior Lecturer in Medicine in the University of Glasgow, 113 pp., Illus., Charles C. Thomas, Publisher, Springfield, Ill., (1953), Cloth,* **$4.50.** This book has been written in response to an invitation to compile a small monograph on the megaloblastic anemias. The book is addressed to the general physician rather than to the haematologist and therefore stresses those general principles which are of clinical importance. Contents: I—The Concept of Megaloblastosis. II—Therapeutic Preparations. III—Addisonian Pernicious Anaemia. IV—Non-Addisonian Megaloblastic Anaemias. V—The Diagnosis of Megaloblastic Anaemia. VI—The Etiology of the Megaloblastic Anaemias. References. Index.

The Handbook of Window Display, *by Nestor Castro, 194 pp., Illus., Architectural Book Publishing Co., Inc., New York, (1954), Cloth,* **$8.50.** Mr. Castro, out of his wide experience as a designer and teacher of window display techniques, gives a lucid, practical and detailed treatise of explicit instructions on how to make best use of show window space. He discusses the principles of design and their application in practice, perspective, lettering, figure and scale drawing, window dressing, color techniques, drapery, dressing mannequins and paper sculpture. Emphasized are the use of display fixtures and backgrounds, lighting effects, papier-mache, miniature models, wire forms, floor plans and elevations, tools and supplies. He gives hints for developing imaginative copy and creative possibilities for attaining striking and profitable results.

A French-English Dictionary for Chemists, *by Austin M. Patterson, Professor Emeritus of Chemistry, Antioch College, Second Ed., 476 pp., John Wiley & Sons, Inc., New York, (1954),* **$6.50.** For this new edition the Dictionary has been thoroughly revised with the aid of all available new vocabularies. Many terms and meanings have been added from chemistry and related sciences and from industry. The vocabulary has grown from 35,000 terms to an estimated 42,000. The chemical nomenclature has been revised to accord with the most recent decisions.

Laboratory Instructions in Microbiology, *by Louis P. Genhardt, Ph.D., M.D., Professor and Head, Department of Bacteriology, College of Medicine, University of Utah, and Dean A. Anderson, M.S., Ph.D., Professor of Microbiology, Chairman, Div. of Natural Sciences, Los Angeles State College of Applied Arts and Sciences, 253 pp., The C. V. Mosby Co., St. Louis, (1954), Paper cover,* **$3.25.** This manual embodies a large number of experiments, many of which have been used repeatedly by the authors in their laboratories. While designed as a companion to "Microbiology" by Gebhardt and Anderson, it can be used very successfully with other texts.

Assay and Detection of Pyrogens, *Reprinted from the Journal of Pharmacy and Pharmacology, 43 pp., The Pharmaceutical Press, London, paper,* **3s. 6d.** *(postage 3d.).* This is a report of a symposium arranged by the Pharmaceutical Society of Great Britain and the Biological Methods Group of the Society for Analytical Chemistry and held on December 11, 1953, at University College, London. The following papers were presented: The Occurrence and Importance of Pyrogens, by T. D. Whittet. Routine Pyrogen Testing, by K. L. Smith. The Leucocyte Response in the Rabbit to Pyrogen from Proteus Vulgaris, by Mary Dawson and J. P. Todd. Rabbit Responses to Human Threshold Doses of a Bacterial Pyrogen, by J. G. Dare and G. A. Mogey. Standards of Pyrogenic Activity, by W. L. M. Perry.

(Continued on page 698)

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(Continued from page 697)

A History of the College of Pharmacy, Columbia University, *by Charles W. Ballard, Deah of the College of Pharmacy Retired, 89 pp., Illus., Columbia University Press (1954), Cloth,* **$2.** In the 1820's a few alert and alarmed pharmacists banded together to take concerted action against the then rampant adulteration of drug materials. From this small group came the official establishment of the College of Pharmacy in 1829. Dr. Ballard traces the history of its change and growth from this beginning as an independent school to its present close affiliation with Columbia University.

The Standard American Encyclopedia of Formulas, *Edited by Albert A. Hopkins, 1077 pp., Grosset & Dunlap, New York, (1953), Cloth,* **$3.50.** This is a revised edition of this standard book of formulas for homemakers, laboratory technicians and anyone who wants or needs to make any of thousands of products. This work contains over 15,000 formulas, recipes and methods in many fields. The contents of this book was compiled from a great mass of technical material built up during the past fifty years in specialized activities. This material is organized—with the convenience of the reader in mind—into twenty-seven chapters alphabetically arranged from "Accidents and Emergencies" to "Writing Materials" plus a comprehensive index which places every formula at hand at a moment's notice.

The Infra-red Spectra of Complex Molecules, *by L. J. Bellamy, B.Sc., Ph.D., Principal Scientific Officer, Ministry of Supply, 223 pp., John Wiley & Sons, Inc., New York, (1954), Cloth,* **$7.** Infra-red spectroscopy is being employed to an ever-increasing extent in commerce and in organic chemistry for the recognition and the quantitative analysis of structural units in unknown compounds. The present work is an attempt to present a critical review of the data on which infra-red spectral correlations are based, indicating the classes of compounds which have been studied in each case and the known factors which can influence the frequencies or intensities of the characteristic bands. The subject-matter of this book has been strictly confined to the empirical interpretation of infra-red spectra, as this is the topic on which no adequate text has appeared.

The Pharmacologic Principles of Medical Practice *by John C. Krantz, Jr., Professor of Pharmacology, School of Medicine, University of Maryland, and C. Jelleff, Professor of Pharmacology, School of Medicine, University of Maryland, Third Ed., 1183 pp., The Williams & Wilkins Co., Ballimore, (1954), Cloth,* **$12.** This is a textbook on pharmacology and therapeutics for medical students, physicians, and the members of the professions allied to medicine. Several changes were made necessary in this third edition owing to the rapid advances which have been made in the medical

sciences. Among these are: an interpretation of the action of drugs at an enzyme level when possible, and expansion of the chapters on antibiotics, tuberculosis, the arthritides, and hypertension. The chapters on rickettsial diseases and the origin of new drugs have been deleted. The essentials of these chapters have been condensed and included elsewhere in the text. The chapter on the treatment of syphilis has been materially reduced. A new chapter on therapeutic aids has been included. To conserve space, drugs no longer generally used have been deleted. Many of the new drugs that have been developed since the writing of the second edition have been included. New illustrations and tables have been used in places throughout the text. Recent references, especially those of review articles, have been added. Lists of the preparations and dosages of the British Pharmacopoeia, have also been added.

Toxicity of Industrial Organic Solvents, (*Revised in consultation with the Toxicology Committee*) *by Ethel Browning, Chemical Publishing Co., Inc., New York, (1953), 411 pp., Cloth,* **$8.** This work is important for industrial safety and for the diagnosis and treatment of acute and chronic poisoning of workers in all plants which use organic solvents in their manufacturing processes. It is a comprehensive report on the effects on animals and man of a great variety of solvents used in industry. The principal aims of the collection and publication of these data is the avoidance of poisoning from the use of the solvents discussed and to facilitate the diagnosis of poisoning and treatment of workers exposed to the toxic effect of the solvents. The book contains 53 important tables, literature references and a detailed index.

PATENT THOUGHTS AND TRENDS

(Continued from page 692)

composition, which incidentally contained also an emulsifier, that was granted a patent.

Relying on the authority of the Wallace case (in which the U. S. Supreme Court invalidated the Arrid Patent) the judge held that the combination of aluminum chlorohydrate with an emulsifier is not invention. Since Andersen's cream was made up of ingredients and proportions in line with earlier formulas the judge felt that it required no special imagination and hence was not patentable.

Nose Uplift Composition Patentable

Posnack and Michaels recently won U. S. 2,689,561 dealing with a preparation and method for raising the nose tip.

One of the allowed claims reads as follows:

A liquid cosmetic preparation for forming a transparent, colorless fluid for holding the skin in molded contour essentially comprising:

Cellulose nitrate (dry basis)	10 parts
Castor oil	5 parts

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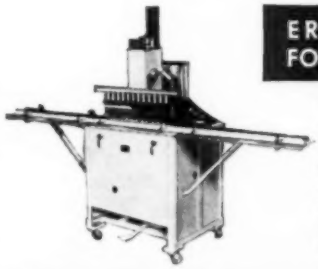

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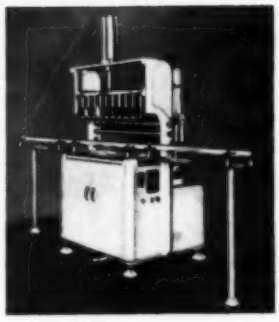

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The method employed was simply to raise the nose tip and while in this raised condition the composition is applied to the tip, the skin being released after the film is formed.

The inventors had a hard time in the Patent Office and had to go to the Board of Appeals before obtaining allowance. One of the grounds of rejection by the Examiner was that the subject matter—changing the contour of the nose—lacked sufficient utility and importance to be considered as warranting the granting of a patent. However, the Board of Appeals disagreed with the Examiner, stating that it thought that changing the contents of the nose can be considered as a matter of beautification or improvement of the features of a person and is of the same utility and importance as the use of other cosmetics, such as lipstick and nail enamel composition. Furthermore, the Board recognized that opinions might differ on this point but the clincher for patentability was the fact that the Board recognized that in the theatrical art raising the contour of the nose is often done and consequently felt that the application of the nose tip raising composition in the theatrical art was sufficiently important for patent purposes.

Air Treating Gels

A novel approach in this art is covered by U. S. 2,691,615, assigned to Airkem Inc.

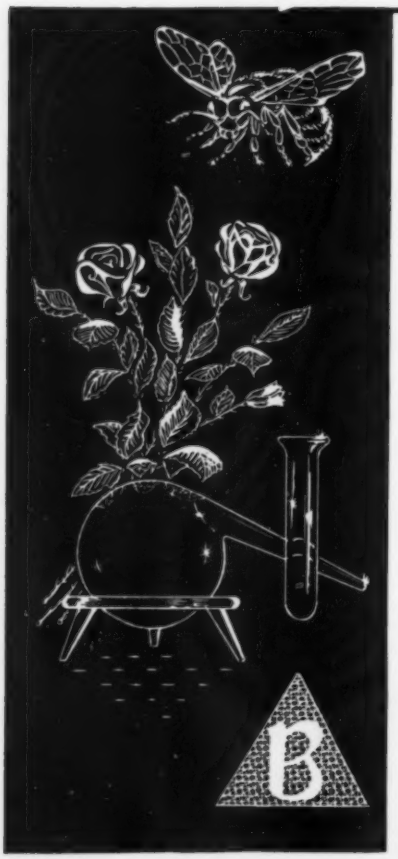
We are all familiar with various means for contacting air-in order to make it more pleasant. Such means involve the use of wick bottles, wick floats, sponges, cartridges, constant level pools, thermal evaporators, etc. The chief problems encountered with such treatments are the difficulty of obtaining a desirable rate of evaporation and the fact that the odor of the first portion of vapor emitted may be distinctly different from that of the last portion.

To overcome such difficulties and to widen the use of air-treating compositions, Turner and Rasko hit upon the idea of making air-treating compositions in gel form.

Gelling agents which can be used include an alginate, nitrocellulose, gelatin, pectin, agar-agar, a gum, such as karaya and gum tragacanth, starch, etc. The gelling agents are present in an amount from one per cent to about four per cent, suitably about 1.5 per cent. The amount of gelling agent should be such as to yield a firm gel substantially devoid of syneresis, or clotting.

The inventors postulate the theory of operation as follows:

The uniformity of diffusion of the liquid from the interior to the surface of the gel is an important factor in influencing the rate of evaporation. This diffusion rate is said to be substantially independent of temperature, humidity, and velocity of the ambient air.



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Furthermore, regardless of the component of the liquid which may be brought to the surface, it will volatilize substantially independently of its association with other components. Consequently the composition of a vapor arising from the gel surface is said to depend primarily on the rate of diffusion to the surface of the various components of the liquid.

Since the evaporation rate is a function of the gel surface and since the gel mass will recede as the liquid evaporates, the inventors suggest cutting or dicing the composition in order to expose more surface as the receding develops, and thereby equalize the surface during the entire evaporation process.

Among the specific fields in which the invention is said to be applicable are the following:

Air Conditioning, household, sickrooms, airplanes, railroad cars, buses, perfumes, dispensers for smelling salts, inhalants and humidifiers.

Permanent Wave Lotion

A Florida inventor, Oliva, obtained U. S. patent 2,691,378, covering hair-waving lotions and methods involving the conjoint use of proteinaceous material and a polyalkylene glycol having at least 400 and preferably at least 1000 recurring groups in the molecule.

According to the inventor, when these two materials are employed in an aqueous alkaline medium capable of softening the hair the glycol permits the proteinaceous material to form a wave of excellence and the presence of the proteinaceous material renders the polyalkylene glycol resistant to removal by shampooing, the resulting wave being resistant to brushing and washing as well.

PHARMACEUTICAL PATENTS

(Continued from page 609)

produce and market the drug with the result that the court action against them was necessary—which action was successfully concluded in favor of the patent owner.

Today we have a somewhat similar situation in the case of tetracycline. A patent application claiming tetracycline, its salts, and a hydrogenation process of making the drug from chlortetracycline (Aureomycin) was filed in October 1952. Lederle filed an application with similar claims in March 1953. Heyden filed an application claiming tetracycline, its salts, and a fermentation process in late September 1953. And Bristol Laboratories filed an application with claims similar to those of Heyden in late October 1953.

Naturally, the filing of these conflicting claims brought about interference proceedings in the Patent Office and delayed for quite some time the issuance of any patent on the drug. The first interference was declared at the end of December 1953 involving a claim to the product, tetracycline, by Pfizer and Lederle. Lederle meanwhile had acquired Heyden's patent but chose to contest the interference with its own application rather than with Heyden's. The Bristol application was excluded from the interference because it had been filed too late to make the claim in issue (more than a year after the Pfizer October 5, 1952 publication in the

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The first interference was settled by an agreement between Pfizer and Lederle. The two companies exposed their dates and Lederle conceded priority to Pfizer. As part of the agreement, Lederle will be licensed by Pfizer to make and sell tetracycline if and when a patent is issued to Pfizer. Also as part of the agreement, Lederle licenses Pfizer to produce chlortetracycline (Aureomycin) for use as a raw material from which to produce tetracycline.

However, after the Patent Office rejected all of Bristol's tetracycline claims on the basis of Pfizer's October 5, 1952 publication, Bristol filed a second application in January 1954 specifically directed to various salts of tetracycline including the hydrochloride. The Patent Office then declared a second interference on the conflicting claims of tetracycline hydrochloride by Pfizer and Lederle (Heyden). This tended to delay the issuance of any patent still longer.

Then a comparatively short time ago, Bristol Laboratories made arrangements to supply E. R. Squibb & Sons and The Upjohn Company with tetracycline hydrochloride for marketing through their organizations. Naturally, the continuance of this arrangement would depend on whether or not a patent was issued to Bristol on tetracycline hydrochloride, or whether or not Pfizer got the patent on tetracycline and its salts.

However, on October 13, the Patent Office granted the motions of Pfizer to exclude Bristol Laboratories and Lederle from the interference. The immediate effect of this decision was to leave Pfizer as the only company in a favorable position to obtain a patent on tetracycline. And if Pfizer obtains a patent on tetracycline, certainly this would appear to include any ordinary salts, such as the hydrochloride, that are made from it.

Before the October decision dismissing Bristol's interference, Lederle sued Bristol claiming infringement of Lederle's 1949 patent on chlortetracycline (Aureomycin). This is believed to be on the basis that tetracycline cannot be produced by fermentation without production of chlortetracycline. It is said that in order to avoid producing chlortetracycline, the process must be kept chlorine-free, and this is impossible. However, if Pfizer were to get a patent on tetracycline, this suit would probably be dropped.

But the point of this whole matter is the apparent lack of respect for possible patent rights that has arisen in this industry within recent years. Is this to become common practice among the so-called ethical drug manufacturers? Legal maneuvers to bring about delay and to muddy the waters in the minds of the medical and pharmaceutical professions are not very nice tactics.

For the good of the entire pharmaceutical manufacturing industry, the less these professions know about the patents in the industry the better. Certainly, the members of these professions are not interested in the right of any one firm to have a patent on an important product which they prescribe. And if a new product

were particularly efficacious in controlling a disease which was a widespread serious problem, the pharmaceutical manufacturer owning the patent might be seriously embarrassed if he tried to become the only producer and marketer of the product. As an example of this, there was the case of the isoniazid patent which was issued to Hoffmann-La Roche. Since this drug was for the treatment of such a serious world-wide public health problem as tuberculosis, Hoffmann-La Roche did not think that it was right to keep this patent to themselves and to Squibb who had been cross-licensed before the discovery dates were exposed. Therefore, they said nothing about the patent, but let word get out that they would license anyone who requested a license. Shortly after, there were upwards of thirty different brands of isoniazid on the market.

But all basically new pharmaceutical discoveries are not specifically for a disease which presents such a public health problem as tuberculosis. And there is no reason why the discoverers of them are not entitled to patent rights on them. For other manufacturers in this industry to cause delay in the issuance of patent rights and to try to gain in the meantime a position with the professions in the marketing of these products is certainly not very ethical. The object is to shoulder one's way into the marketing of a product by sheer force. The point of establishing one's position in a product, before the patent is issued, is that the originator might be afraid of criticism from the professions if it refused licenses to any of these companies after the patent had been obtained.

It seems time that the manufacturers in this industry stopped to consider where continuance of such competitive tactics will lead it. While this country owes a greater part of its growth to the patent system, there are many forces at work in this country which seek to destroy this system. And certainly if any nibbling at the edges of the system is to take place, it will start on patents on products for the maintenance of health. It is no idle dream to predict that if the application of the patent system to pharmaceutical products gets wide and proper airing throughout this country, the end of pharmaceutical patents might come about. And one way to start a proper airing of the pharmaceutical patent situation is to cause the medical and pharmaceutical professions to start talking about it. The first thing the industry knows, abolishment of patents to pharmaceutical products will become the subject of a bill in Congress as well as a plank in the platform of one of the national political parties.

MASCARA AND EYE MAKE UP

(Continued from page 617)

may be made easier. The ratio of waxes to soap would vary with the amount and type of pigments incorporated, since they vary as to the raising of the melting point required to keep the bulk free-flowing after the grinding of the pigments into the vehicle. Too great a concentration of triethanolamine stearate would raise the melting point of such a mixture. If it is found

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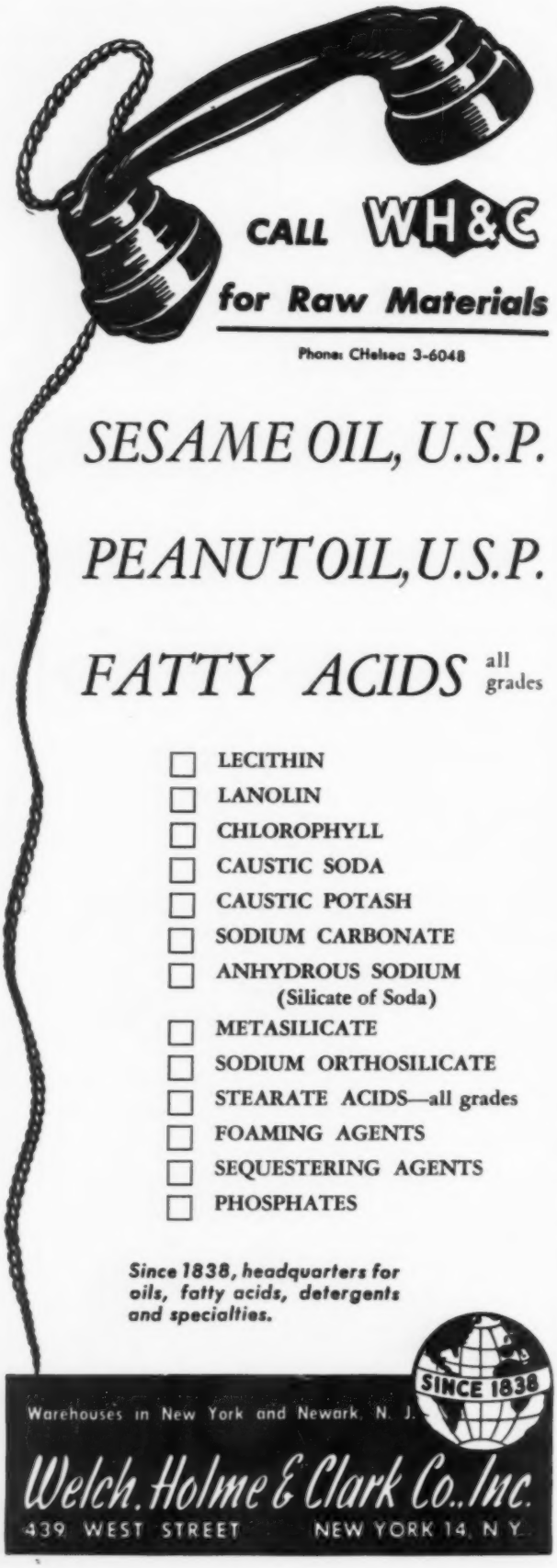

necessary to lower the melting point the soap of a lower fatty acid may be desirable. To insure easy flowing the wax phase should be the largest present in the system. It is further inadvisable to use a pigment concentration in excess of 10 per cent unless the pigments are easily wetted by the oil phase.

After grinding, the mass is usually melted and stirred to remove any incorporated air and then poured into molds. In examining the characteristics of the product the emulsion formation with trituration should not be too easy. The best measure would be the opinion of a woman who ordinarily uses this type of mascara.

Cream mascaras are also quite common. In this product the water has already been incorporated to provide a mascara ready for use without previous trituration. There are some advantages in this type of preparation since a much higher concentration of pigment could be incorporated here than is possible in a cake. In addition the optimum amount of water may be added rather than leaving this to the discretion of the consumer which would be the case in using the cake. The manufacturing process is also considerably cut down, since there is no necessity to pour into molds or to remove the hardened cake from the molds.

The difficulty lies in preparing a cream of the proper consistency and keeping its physical constants the same over a long period of time. The tendency towards dehydration is so great that the only practical container is a collapsible tube. The cream must necessarily be extremely soft—almost watery. Attaining this goal, and still keeping the cream stiff enough to allow it to be filled into tubes readily, is not easy since many of these emulsions have a tendency towards stiffening on long standing, thereby making application difficult.

Grinding of the pigments into the emulsion, however, is easier, since the cream does not have to be kept warm for this to be accomplished.

Since mascaras are not usually cosmetics that are used daily, as are lipsticks, they last over a long period of time. Without having any statistics on hand I would estimate that the average purchase per user would be about once per year. It therefore becomes necessary to be sure that the product will keep its functional and physical characteristics under the conditions of use for this long a period.

Eye shadows are not in as general use as are even the mascaras, but there is enough of a demand to keep manufacturers supplying them. As in mascaras, choice of colors is limited to carbon blacks, ultramarine blue and the various yellows, browns and reds exemplified by the iron oxide pigments. There is usually a higher concentration of pigments used here as compared to mascaras, running as high as twenty five per cent. The vehicle into which the colors are ground usually consists of beeswax, ozokerite, mineral oil and lanolin, if desired.

The method of manufacture consists of melting the waxes and oils together and then adding the colors and titanium oxide—usually used to impart the desired opacity—and grinding through a roller mill. The mass

is then heated again with stirring to remove occluded air and then poured into this container. If a sheen is desirable, subsequent flowing of the surface is also recommended.

In formulating the shades, one of the carbon blacks is used for black, ultramarine for blue and mixtures of the iron oxide for brown. The availability of the umbers, siennas, ochers and red oxides provides a means of attaining any of the desired effects. Grays may be made by mixing ultramarine with titanium oxide, by mixing a carbon black with titanium oxide or by use of all three, depending on which gray is the desired hue. Violets may be attained by ultramarine blue with red oxides and greens by using red oxides and ochers.

There have appeared in the past—and there may appear again—eye shadows with a metallic luster. These may be made by incorporating finely ground aluminum or bronze powders.

The eye make ups in general represent a classification in which no great interest has been shown technically. This may be due in part to a gradual decrease in their use. There is enough of a demand for these products, however, to keep the manufacturers supplying them. They cannot look forward to a large increase in this facet of cosmetic sales, though, unless there is a radical fashion change—which is always possible.

THE ROLE OF DRUGS IN NUTRITION

(Continued from page 624)

enzymes, hormones, and other factors such as the nervous system.

Nutrition Therapy

Up to now I have spoken largely of investigation in nutrition physiology. A topic that I should like to treat further is the concept of therapeutic nutrition. Severe illness, trauma, and other forms of stress may profoundly alter the body's metabolic demands. In major trauma such as surgery, the system tends toward a catabolic economy suggesting that of starvation. Negative nitrogen balance and the virtual disappearance of ascorbic acid from the circulation are common. In convalescence, similar changes, such as negative nitrogen and calcium balance, may occur. Whereas these conditions can be controlled to some extent through elevation of nutritional status, a better understanding of their etiology would lead to improved techniques.

There is evidence that high-protein, high-caloric diets administered following injury, and especially during convalescence, decrease complications and speed recovery. The precise requirements for vitamins in trauma and disease are unknown, but supplements are recommended, especially in severe cases. In certain pathologic states, water and salt are administered according to reliable standards. But a great deal remains to be learned. Urgently needed, for example, is information on vitamin and electrolyte requirements, the place of hormones in treatment, and the role of labile

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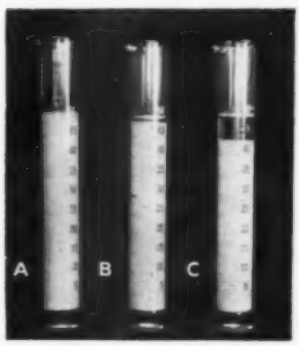

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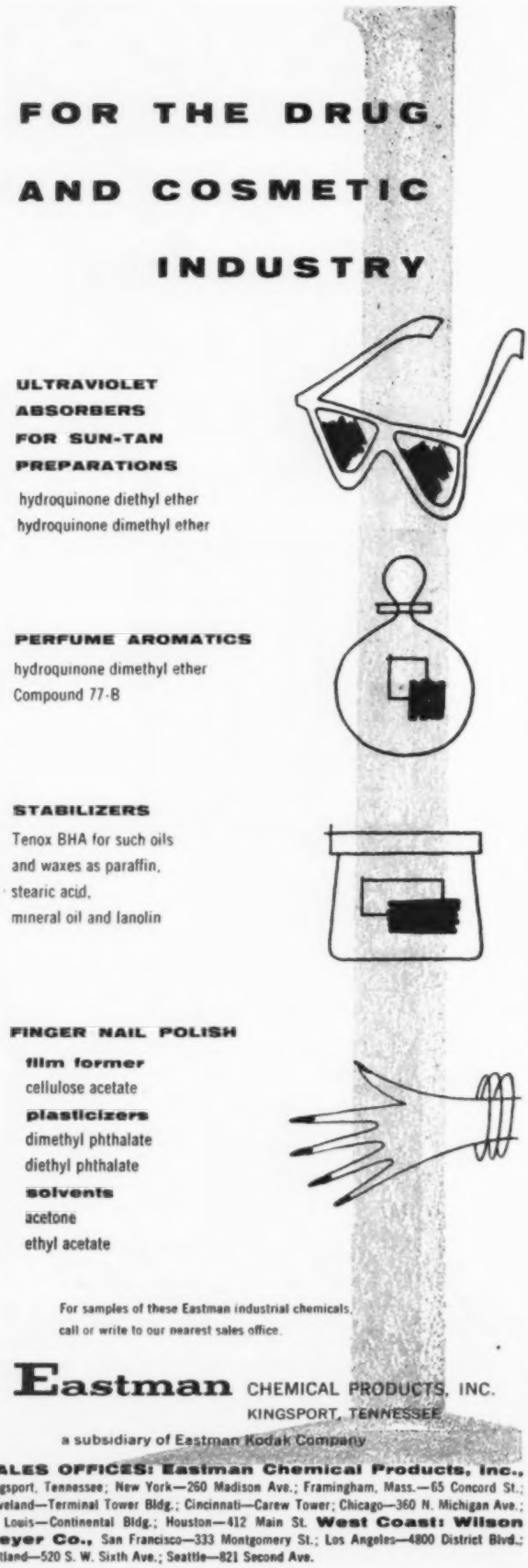

proteins in response to injury. Further biochemical studies at the laboratory and clinical levels are indicated.

Pharmacological research has yielded much literature, largely controversial, on the therapeutic effects of nutrients in disorders apparently unrelated to dietary deficiencies. The doses are usually massive compared with dietary needs. I have discussed the use of pyridoxine in isoniazid-induced neuritis. As illustrations of promising research leads, I shall mention a few more such effects of vitamins, beginning with those of the B complex.

Niacin stimulates the secretion of stomach acids and induces dilation of peripheral blood vessels. Because of the latter property, niacin or derivatives are sometimes used in treating vascular disorders, such as frostbite, arteriosclerosis, and certain types of headache. Brominism has been reported to respond to niacin therapy, and one derivative of niacin is widely used as a respiratory stimulant. The niacin, relative, isoniazid, was developed following reports that niacinamide inhibited experimental tuberculosis—an unexpected dividend of nutrition research.

Vitamin B_{12}, ordinarily injected in minute doses for pernicious anemia, is beneficial at 50 to 200 times those amounts in cranial nerve neuralgias and diabetic neuritis. Spectacular results of B_{12} therapy in neurological disorders of alcoholism have recently been described. In animal studies, preliminary findings indicate that B_{12} may also promote wound healing.

Among the best-established pharmacological effects and uses of the other B vitamins are the following. Para-aminobenzoic acid, an essential part of folic acid, reduces the severity of rickettsial infections and maintains the blood levels of salicylates in rheumatic fever. Thiamine is used to stimulate the appetite. The side-effects of choline resemble the actions of three other drugs—muscarine, nicotine and curare. In studies on tumor-bearing animals, alternate restriction and supply of riboflavin or pantothenic acid has appreciably prolonged life. Pyridoxine is useful in radiation sickness and the early nausea of pregnancy, and pyridoxine or folic acid has been shown to influence the mortality of irradiated mice.

Turning to vitamin A, we find that near-toxic doses have benefited patients with a variety of skin disorders, such as the hereditary Devergie's disease. In many cases of these conditions, blood levels of the vitamin prior to treatment were normal.

Among the known nutrients, vitamins C and D have probably been credited with the widest range of uses. They are claimed to be valuable in the treatment of arthritis, hay fever, asthma, and various dermatoses. In addition, vitamin C has been reported effective in radiation sickness, peripheral arterial disease, metal and barbiturate poisoning, drug sensitivity, diabetes, muscular fatigue, rheumatic fever, and certain blood dyscrasias. Other conditions said to respond to vitamin D therapy are nonpulmonary forms of tuberculosis, toxemia of pregnancy, and the bleeding tendency in ob-

structive jaundice. Incidentally, much of the literature on vitamin D toxicity derives from such studies.

Most of these claims for vitamins C and D, and for other nutrients I have not discussed, are unestablished, and many have been denied. This is not to say, however, that a broad spectrum of pharmacological effects has not been observed. It is this fact that I wish to emphasize, if only in passing. Undoubtedly, the mechanisms of those effects constitute a field for exploration that could yield important practical results.

In the area of therapeutic nutrition, one other topic should certainly be mentioned—intravenous alimentation. Complete intravenous feeding, long a goal of medical science, appears to be almost realized. Amino acids can be obtained in sufficient amounts at prices within reach, and the carbohydrate, vitamin and mineral requirements do not present insuperable difficulties. The main remaining problem, which is now under study, is that of developing nontoxic emulsifiers and fat emulsions with the necessary stability and other properties for intravenous use.

STEROID HORMONES IN MEDICINE

(Continued from page 621)

more active than DCA in tests employing sodium retention as the criterion of potency. The Princeton group using crystalline material supplied by Reichstein, found the average maintenance dose of aldosterone to vary from 6.2-12.5μg/dog/day when given in 10 per cent aqueous alcohol to adrenalectomized dogs. It was 12-25 times more active than desoxycorticosterone solubilized in a similar manner, and 30-50 times more potent than DCA when the latter was administered in oil. By comparison, the minimum maintenance dose of solubilized cortisone and hydrocortisone for dogs lacking adrenals was 5000μg/dog/day. This is 500 times the maintenance dose requirement for aldosterone.

The newly isolated steroid differs physiologically in certain respects from DCA: 1) It is far more potent in retaining sodium; 2) It is less active than DCA in stimulating potassium excretion; 3) It has been reported that aldosterone is 30 times more active than DCA in increasing the liver glycogen of mice. Gaunt found it as potent as cortisone when used on rats in the cold-stress test but it appears to be weaker than cortisone in the eosinophil depletion test. The reviewer is familiar with but one detailed published clinical trial of this steroid. It proved to be highly effective in rendering two Addisonian patients symptom-free and the required dose varied between 150-200μg (2.5-3.3μg/Kg./day). The symptoms disappeared a few hours after treatment began and no signs of edema or other evidence of toxicity appeared.

In a paper as yet unpublished, Simpson and Tait have made some interesting observations on aldosterone in Man. They found that the level of circulating steroid per 100 cc. of whole blood is approximately 0.08μg and that 20μg administered to a normal man will markedly depress the Na/K rates in salivary secretion in 2.5 hours. Finally they showed that aldosterone is as

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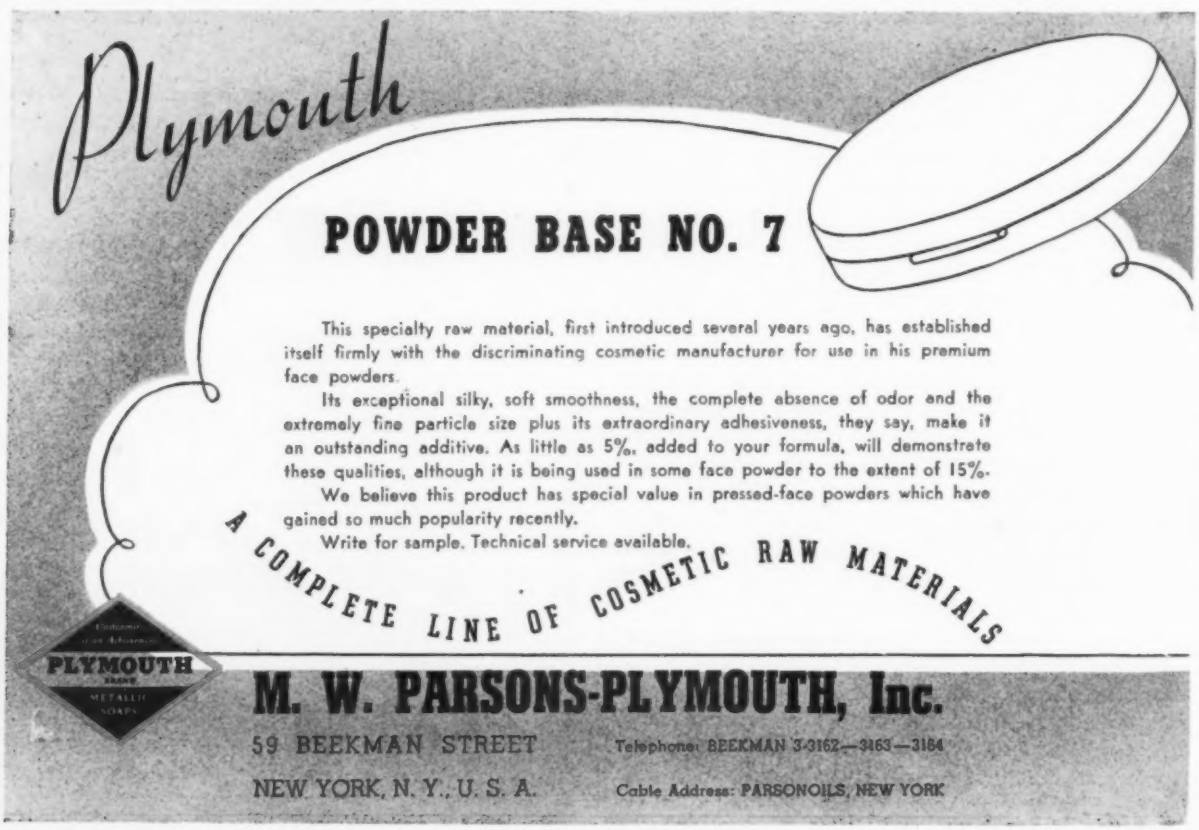
effective when given orally as when given by vein and that 80-100μg/day orally controls sodium and potassium levels of the blood in the Addison's diseased patient. Patients with rheumatoid arthritis have been given 200, 400 and 800μg/day for six days. Apparently there was no amelioration of symptoms during this interval. However, there was a moderate increase in weight indicating water retention.

Today hundreds of thousands of dollars are being spent by the pharmaceutical industry, e.g., Ciba, Merck and The Upjohn Company in an effort to synthesize aldosterone and make it available to the clinician as quickly as possible.

The demonstration by Hench, Kendall, Slocumb and Polley that cortisone exerts dramatic therapeutic effects on rheumatoid arthritis patients, initiated a new era in adrenal hormone therapy. Prior to their announcement, cortical steroids had been shown to be of great value in the treatment of Addison's disease but their efficacy in other disabilities remained unproven or of questionable value. Today few fields of medicine or physiology are more active than those concerned with studies of the functional significance of cortisone in health and its therapeutic value in disease. In spite of the enormous volume of clinical and laboratory data collected, the essential function of cortisone and the other C_{11}-OXygenated adrenal steroids remains unknown. Their action is so widespread, so ubiquitous and covers such an astonishing range of biological functions that our present-day knowledge concerning them is still too fragmentary to permit one to formulate an all embracing theory of their primary function and locus of action.

The physiological activity of those adrenal steroids such as desoxycorticosterone which lack an oxygen at C_{11} differs from steroids such as cortisone and hydrocortisone which have an oxygen at this position. These two compounds exert little control of electrolyte and water distribution but instead are active in functional areas such as regulation of certain aspects of organic metabolism where the desoxy compounds are relatively inert. The lantern slide illustrates the differences in the type of functional activity displayed by desoxycorticosterone and cortisone. Thus cortisone plays an important role in the intermediary metabolism of carbohydrate, stimulates gluconeogenesis, inhibits undue utilization of glucose, maintains the work capacity of skeletal muscle, exerts strong anti-insulin effects, prevents the occurrence of hypoglycemia in fasted Addisonian patients and influences the metabolism of protein and fat. This steroid also increases resistance to stress, maintains the functional reactivity of the peripheral vasculature and suppresses inflammatory reactions of connective tissue. Overlapping of function does occur between the desoxy type of steroid and the C_{11}-OXygenated type. This is illustrated by aldosterone and especially by the 9α-halo derivatives of cortisone and hydrocortisone which exhibit the functional activity characteristic of both steroid types.

The surprising adrenocortical activity of these 9α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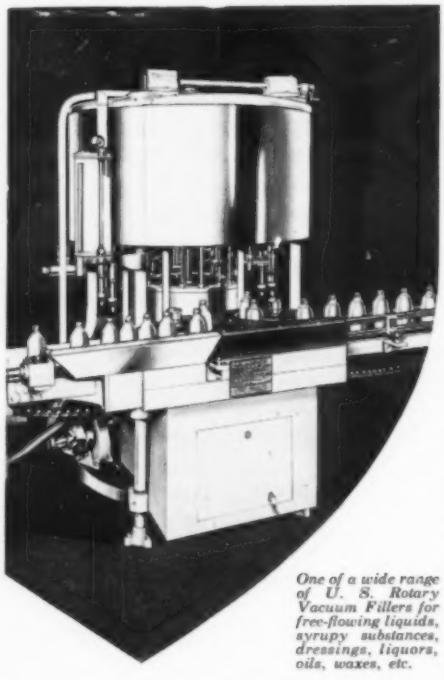
halo derivatives of cortisone and hydrocortisone is another new and highly important development in the field of adrenal steroids, made all the more interesting because these compounds are man-made modifications of the natural steroids and apparently superior in potency to the secretion of the cortex itself. This series in which the 9α-hydrogen atom is replaced by halogen, was prepared and tested by Fried and Sabo in the laboratories of E. R. Squibb & Sons. Some of these compounds have the distinct advantage over the parent steroids of possessing both sodium-retaining and carbohydrate activity in high degree.

Borman, Singer and Numerof, also of the Squibb Institute, examined the series for physiological activity and report that the Chloro-F-Acetate was 10-20 times more effective than DCA in stimulating growth and survival of adrenalectomized rats and in sodium retention tests it proved to be 10.8 times more potent than DCA. The parent steroid, hydrocortisone, has little activity in stimulating sodium retention except in enormous doses. Perhaps the most interesting observations of these investigators was the demonstration that the Fluoro-F-Acetate and Chloro-F-Acetate are many times more potent than cortisone in their effects on certain aspects of carbohydrate metabolism, i.e., deposition of liver glycogen. Thus the glucocorticoid potency of these 9α-halo derivatives of cortisone and hydrocortisone is not only greatly enhanced by the halogen but the mineralocorticoid activity is also multiplied many times.

The Chloro-F-Acetate and Fluoro-F-Acetate were recently assayed in my laboratory on adrenalectomized dogs. The minimum maintenance dose required each day to hold the arterial pressure, body weight and serum electrolyte levels normal was 55μg/dog/day for Chloro-F, and 27μg/dog/day for the Fluoro-F. On the other hand the daily requirement for the non-halogenated cortisone and hydrocortisone was 5000μg per day. The minimum maintenance dose of DCA was approximately 250μg per day. These figures serve to give some idea of the greatly enhanced potency of the 9α-halo compounds.

To my knowledge, but two clinical tests of these new derivatives of cortisone and hydrocortisone have been reported to date. Thorn and coworkers compared the potency of the Chloro-F-Acetate with hydrocortisone in a variety of metabolic and clinical studies in both Addisonian and non-Addisonian patients. Qualitatively the effects of the two compounds were the same. The Chloro-F-Acetate proved to be much more potent than hydrocortisone in tests involving circulating eosinophils and on the renal excretion of sodium, potassium chloride and uric acid. Only small doses were required to maintain the Addisonian patient. Tests of the Fluoro-F-Acetate revealed that 250μg per day given orally was sufficient to maintain the Addisonian patient in a near optimum clinical state.

Liddle and Associates in work on adrenalectomized dogs found the Chloro-F-Acetate to test much stronger than desoxycorticosterone or hydrocortisone and state



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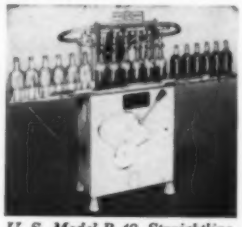

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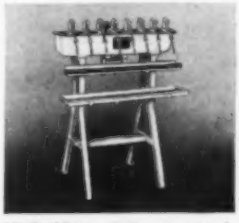

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that clinical studies confirmed the potency of compound. These drugs require further study with special reference to dosage and toxicity. Insofar as animal experimentation goes, no evidence of disabling toxicity has appeared. This has been the experience of the workers at the Squibb Institute, using adrenalectomized rats and normal dogs and the Princeton group, employing adrenalectomized dogs. According to workers in the Squibb Institute when doses of 750μg/Kg./day are administered over extended periods the dogs develop a diabetes insipidus-like syndrome and may eliminate 3-4000 cc. of urine per day and ingest similar quantities of water. Despite this "water diabetes" the dogs remain active, vigorous and are otherwise free from symptoms.

Cortisone has been tested clinically on about every disease to which Man is subject and a surprising number of diseases respond favorably, for a time at any rate to the cortisone therapy. The symptoms are suppressed, the patient feels much better and may consider himself on the high road to complete recovery. Unfortunately, however, these steroid hormones in most cases, although suppressing symptoms apparently leave the basic disease process unchanged.

THE CLEAR SHAMPOO

(*Continued from page 611*)

Control

In dealing with almost every type of cosmetic at least three aspects of product stability must be examined and evaluated; namely, chemical, physical, and bacteriological. At least the two former and possibly the latter apply to shampoos. Practically anything can go wrong with a shampoo—milky shampoos separate, egg shampoos may coagulate, clear shampoos may cloud up, viscous shampoos become watery, pearly shampoos settle, paste shampoos may be soupy or even set up to a solid, or as can happen to all of them, the perfume might go off odor due either to chemical or bacterial action. At any rate, adequate controls should be set up to insure product uniformity and stability.

The pH should be taken immediately upon completion of a batch of shampoo. This value will fluctuate with the type of shampoo manufactured so that the desired pH must be set by the technician after rigid examination.

A composite sample should be taken and divided into three portions, one of which is subjected to a temperature of 100° F. for 15 days, a second is chilled to 20° F. to 35° F. for 15 days, and the third portion is used for the following tests:

A small sample is placed on a microscope slide and examined under low power. Any deviation from normal crystalline structure or particle size should be noted.

If the shampoo is a liquid cream, a sample is placed in a tube and vibrated for six hours. If the emulsion is unstable, this operation will accelerate separation.

A color comparison is made between a sample of the test shampoo and a predesignated standard.

Viscosity should definitely be determined either by use of the Gardner bubble apparatus or another reliable device. Many shampoos tend to be somewhat thixotropic, and in such a case it is best not to use a Braebender or, other viscosimeter, equipped with an agitator as the paddle has the temporary effect of making the shampoo less viscous.

An excellent method of viscosity determination is by the use of a plastic viscosity cup with a known aperture. The time, in seconds, for the cup to deliver a designated amount, i.e., 50-60 ml., is taken as the viscosity value of the shampoo.

A great difficulty encountered in the manufacture of a clear liquid shampoo is clouding, and some effort must be made to guard against this trouble. It is very difficult to get an accurate cloud point on any product, as varying conditions will greatly affect the value received. Hence, it is highly possible that the same technician, running a cloud point on the same sample a second time, might not duplicate the first reading.

The best method for cloud point control is simply to set up a water bath containing an immersion heater and a copper or aluminum coil through which cold water should be run. A temperature of 50° F. ± 0.5° should be maintained, and a sample immersed in the bath for eight hours should show no evidence of clouding.

Another important phase of control is the foam test for, as was previously stated, a shampoo must foam well to be a good seller. A simple procedure for the determination of foaming power follows:

One milliliter of the shampoo to be tested is pipetted into a one-liter, glass-stoppered, graduated cylinder. The volume is brought up to one hundred milliliters with distilled or deionized water. The cylinder is inverted ten times, and immediately upon completion of this shaking a stop watch is started. At the end of one minute the volume is recorded; at the end of three minutes the volume is once more recorded; and, after five minutes has elapsed, the volume is recorded again. These three values are then compared with three previously determined standards.

The pH and viscosity should be determined after prolonged stability tests and compared to the original pH obtained before the test was initiated.

In any case, worthy products cannot be obtained without the careful control of raw materials, careful formulation, maintenance of close tolerances in manufacturing technique, and rigid control of the finished product.

Soap Shampoos

Contrary to some beliefs, soap shampoos can be used in hard water just as easily as detergent shampoos, providing that certain agents are added.

The addition of water softening agents in soap shampoos is very widely practiced. These agents form complexes with otherwise insoluble calcium and magnesium salts rendering them soluble, thus enabling the

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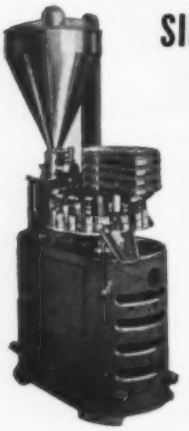

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shampoo to function in hard water as well as it does in soft water. A typical compound used for this purpose is a neutral or slightly alkaline salt of ethylenediamine tetra-acetic acid.

When a soap shampoo is properly made, it should be established that a relatively small amount of free alkali is therein contained, and likewise established that the oils in the shampoo are completely saponified. This can be ascertained by titration with 0.1/N NaOH to positive phenolphthalein, reflexing for 45 minutes, and then back titration with an acid. The comparison of the two values will reveal whether or not the oils are completely saponified. Generally one can judge whether or not saponification is complete simply by heating the soap until a clear product is obtained. A clear soap can generally be considered completely saponified.

The influence of impurities in the oils used to make the shampoo can be terrific, for even in oils obtained from the same source, differences in the saponification value of as much as ± 60 points will sometimes be found. For this reason, it is essential to keep accurate controls on all raw materials received from venders, including caustic soda, or potash, whichever is used.

Three methods of soap manufacture are currently in use, the most popular being termed the Boiled Process. This method is very simple, and at the same time very reliable. The oils, fats, and alkalies are merely boiled together until complete saponification results. The second method is the Heated Process, wherein the exact amounts of the fats and alkalies are mixed and heated. Once saponification has started, the heat is removed, and the mixture is agitated and allowed to complete its own saponification.

The third method is known as the Cold Process. Here the alkali is calculated slightly short of the amount required for complete saponification. The fats, oils, and alkali are mixed in a warmed kettle and agitated at high speed. Saponification automatically takes place due to the heat of reaction. Some 240° F. is reached during this reaction.

Such oils as coconut, palm, olive, castor, cottonseed and almond are used, while the alkali most often used is sodium or potassium hydroxide. Triethanolamine is sometimes added to a shampoo, as it tends to reduce somewhat the irritating properties of the soap.

It is impossible to set down on paper a formula for soap shampoo, since purity of raw materials will always vary, thus leading to either unsaponified soaps or high free alkali content. For this reason a short resume is given to acquaint the technician with the method of formulating a soap.

I. $$\frac{\text{Equivalent weight of alkali used} \times 1000}{\text{Saponification value}} = \text{Equivalent weight}$$

II. $$\frac{\text{Equivalent weight of alkali} \times \text{weight of oil to be saponified} \times \text{purity of the alkali}}{\text{Equivalent weight of oil}} = \text{Weight of commercial alkali required to saponify a given weight of oil}$$

No. 6
SOAP SHAMPOO

1. Oleic Acid	50 parts by weight
2. Coconut Fatty Acids	40 parts by weight
3. Triethanolamine	54 parts by weight
4. Propylene Glycol	50 parts by weight
5. Tetra Sodium Ethylenediamine Tetra-acetate	4 parts by weight
6. Water	800 parts by weight

Heat 1, 2, 3, and 4 to about 65° C. with continuous agitation. Mix until uniform. Add 5 and 6 with enough mixing to give uniform solution but not sufficient to whip air into it.

No. 7
SOAP SHAMPOO

Oleic Acid	55 parts by weight
Coconut Fatty Acids	40 parts by weight
Triethanolamine	58 parts by weight
Propylene Glycol	52 parts by weight
Tetrasodium Pyrophosphate	12 parts by weight
Water	1000 parts by weight

Use the same procedure for manufacture as No. 6 above.

Coconut oil is a favorite ingredient of a great many soap shampoos for it lathers very well, and the public believes a copious lather makes a better shampoo. Actually, a concentrated coconut oil shampoo is irritating to the scalp.

Various proportions of sundry sulfonated oils in one or another degree of sulfonation are, at times, added to a soap shampoo. The sulfonated oils are detergent-cleaners but very poor latherers. They are readily soluble in water and are easily removed from the scalp and hair by water rinsing. A great deal of the action of the sulfonated oils depends upon their ability to act as emulsifiers. They also act as dispersing agents and make excellent vehicles for use in Tar shampoos.

Following are several shampoo formulae designed to illustrate various types of soap systems and additives.

No. 8
COCONUT OIL SHAMPOO

Olive Oil	3.0 per cent
Coconut Oil	21.0 per cent
Caustic Potash 85 per cent	4.1 per cent
Caustic Soda 95 per cent	1.9 per cent
Alcohol	15.0 per cent
Distilled Water	54.0 per cent
Perfume	0.5 per cent
Ethylenediamine Tetra-acetate DiSod.	0.5 per cent

The Cold Process may be used in this case. Simply dissolve the alkalies to make a 50 per cent solution, melt fats and oils together, and allow to stand until they are slightly above room temperature, pour the alkali solution into the oils in a thin stream with constant stirring. The perfume may be dissolved in the alcohol and added in this manner, and the stirring should be continued until the soap is a crystal-clear amber. Allow the soap to stand overnight, then add balance of the required

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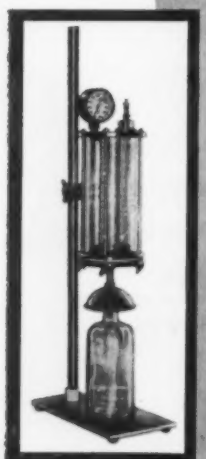

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amount of water. Age for two weeks. Chill to 40° F. for two days and finally filter.

Alcohol has a different effect in soaps than it has on water. Instead of lowering the freezing point of soap, it tends to assist in caking. Alcohol does, however, cause an increase in the viscosity of a soap shampoo, and obviously there is some reason for its use, as it is quite popular in many shampoos.

Alcohol also assists in the saponification of the foregoing soap, for the oils and alkali, brought together in a neutral solvent, will saponify almost instantaneously.

No. 9
OLIVE OIL SHAMPOO

Olive Oil	9.9 per cent
Palm Oil	5.1 per cent
Coconut Oil	7.0 per cent
Caustic Soda	4.4 per cent
Caustic Potash	1.1 per cent
Alcohol	2.8 per cent
Water	68.7 per cent
Perfume	1.0 per cent

This formula can be made by the Hot Process: Dissolve the potash and soda in 30 per cent of the water and heat the oil mixture to 130° to 140° F. Pour alkali solution in a thin stream into oils and agitate while heating to 160° F. Remove from heat and allow it to stand overnight. Add alcohol, water, and perfume; age, chill to 32° F. Finally filter the soap and if desired add up to three per cent of sodium tripolyphosphate to insure clarity.

As outlined by F. Chilson,[1] if a shampoo is properly aged, chilled, and filtered, there should be no turbidity in the finished product, for if turbidity results after filtration, it can be due to any one, or a combination, of six basic causes. These are:

1. The use of impure water.
2. Insufficient aging before filtration.
3. Insufficient saponification.
4. Presence of unsaponifiable foreign matter.
5. Failure to chill before filtration.
6. Carelessness in manufacturing technique.

So that by following a sensible procedure, such as using distilled or de-ionized water, aging for two weeks, and siphoning off the clear liquid so as not to disturb the sludge at the bottom, refrigerating at 32° F. to 38° F. for several days, and finally filtering the shampoo, there is no reason whatsoever for a shampoo to become turbid.

[1] F. Chilson, MODERN COSMETICS, 2nd Ed., 294

ANIMAL SKIN FOR TESTING CHEMICALS

(Continued from page 619)

Certain types of chemicals, as for example the organic amines, do more subcutaneous damage than would be expected from the appearance of the epidermis. Elaborate methods for conducting and evaluating dermal studies have been published and I am sure that this group is familiar with them. Most of these, however,

apply to one objective only and it is of fundamental importance that the biological scientist design and evaluate his program in such a manner that he obtains the answer to the specific question under study. To be led astray by following methods applicable to other objectives is perhaps the most common mistake that one sees in this field, particularly by those lacking fundamental training and experience to whom skin studies look so simple.

While discussing the subject of irritation I should like to digress somewhat from the skin and say that we feel the combination of eye and dermal studies is often more revealing than either study alone. This is particularly true when one is investigating a series of compounds or various concentrations and vehicles for the same compound. We have observed that the reactions in the eye and in the skin sometimes correlate and sometimes are quite opposite. Another aspect of comparative testing which I think has not been adequately developed is that of employing repeated daily application to both the skin and the eye. This is in effect an evaluation of the skin exhaustion capacity and is revealing in some cases. It is not unusual to find, when running parallel series on different compounds, that one compound or one formulation will cause no more reaction after many days of application than it caused on the first application, and the reaction may in fact become more mild. On the other hand, a second material or formulation will cause practically no irritation during the first several days and then, either abruptly or gradually, increase in degree of irritation produced. Studies such as this can conveniently be conducted only in animals if large numbers of chemicals and multiple conditions are to be evaluated in any type of a mass scale. Time, economics, and availability of almost unlimited subjects militate strongly for the use of animal rather than human panels for investigations such as these.

In actual practice the use of animals serves a very important function in screening candidate materials for eventual human tests. While it is true that there is a statistical chance that a valuable candidate may be passed over, this is a calculated risk, and certainly the risk is nowhere near as great as would be experienced if human testing only, with all of its multiple limitations, were used.

Perhaps the most confusing application of animal testing is in the field of evaluating sensitization. I should like to say at the outset that our staff members have had appreciable experience with the various sensitizing techniques in animals. I should also like to add that we do not believe any technique is completely reliable for the determination of sensitizing potential. From the time of Landsteiner, the literature is replete with discussions of sensitization in animals. Many of these papers cover such aspects as the species of animal, the purity of breed, the Mendelian characteristics, the age, the sex, the diet, the method of application, the frequency of application, the number of applications, the interval of challenge exposure after sensitizing ex-

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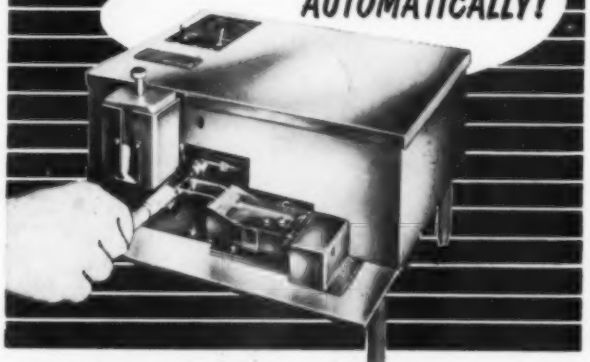

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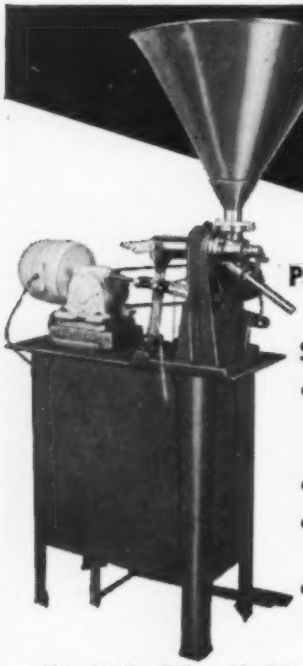

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posure, and countless other variables. It seems to be self-evident that if sensitization in animals were a reliable phenomenon the attention would be spent on studies involving sensitization as an established entity rather than to the discussion of the variables which tend to explain away the negative result.

The above is not meant to say that true sensitization does not occur in animals. I am sure that most of us in the field have seen true sensitization, but the interpretation from animals to humans is extremely inconsistent and unreliable. Most of us also know of examples, published or unpublished, where animals have not reacted as humans have, and vice versa. Here again, the objective is an extremely important consideration. We do feel that new materials, particularly new individual chemicals, should be screened for strong sensitizing potentials in animals prior to human exposure. Our final evaluation on this subject is that if animals are sensitized we are extremely cautious with that material in humans. Certainly it is a suspect chemical until proved otherwise. On the other hand, a negative result in animals serves only to indicate that the chemical is probably not a strong inherent sensitizer and that with reasonable caution we should not obtain severe sensitizing reactions in humans.

The evaluation of aesthetic benefits on animal skin is obviously a long jump and, by and large, is not correlated with the human results. Experienced operators learn to evaluate subjective appearances such as tone, texture, color, and sheen. However, this is still only a guidepost to human reactions since animal skin is normally much more constant in appearance than the human skin. Certainly the application of a cosmetic formulation to the soft, smooth pink skin of the freshly clipped rabbit gives one no real idea of what that same formulation might do on the sun-tanned, wind-roughened facial skin of the human being. Certain cosmetic properties can be evaluated under these same sets of circumstances. For example, although the rabbit skin is deficient in melanin and does not tan under excessive exposure to ultraviolet light, it does react with edema and erythema and hence it can be used for comparing the efficacy of sunscreen candidates. Such a screening program is purely mechanical, however, and would not give one a clear-cut insight into ease, degree, and color of suntan to be achieved in the human with such a candidate compound. This is an example of carefully delineating the objective, knowing the possibilities and limitations of the animal experimentation, and exploiting the method to its fullest without being misled as to its eventual application.

To the extent that cosmetic effects include the healing of superficial cuts, scrapes, and abrasions, these properties can be evaluated in animal skins under controlled conditions. Keratin staining and discoloration can be evaluated, as can the degree of roughening or sloughing under conditions of repeated application. These, then, do give us some examples of evaluation of the cosmetic effects, but certainly the final answer must come from the eventual user of the cosmetic and not from the rabbit.

As is frequently pointed out, methodology is the big void in our present approach, not only to animal but also to human evaluation of skin reaction. More adequate methods of evaluating vascularity, color, smoothness, reflection or gloss, pH, and even chemical composition of the superficial layers are obviously necessary. The use of radioisotopes is one new method which is beginning to find application. This method may eventually find its proper place in the cosmetic evaluation scheme. I should like to caution, however, against overenthusiasm for it in the cosmetic field, lest we not profit from the experiences in the related fields of biochemistry, pharmacology, and therapeutics. The technical traps are many and dangerous and perhaps the greatest of these problems is that of interpretation. I am sure there are those attending the seminar who are more qualified to discuss this subject than I am, though I mention it here primarily to be sure that it is included in the discussion agenda. It is probable that, as radioisotope techniques develop, animals will play a very important part in the application.

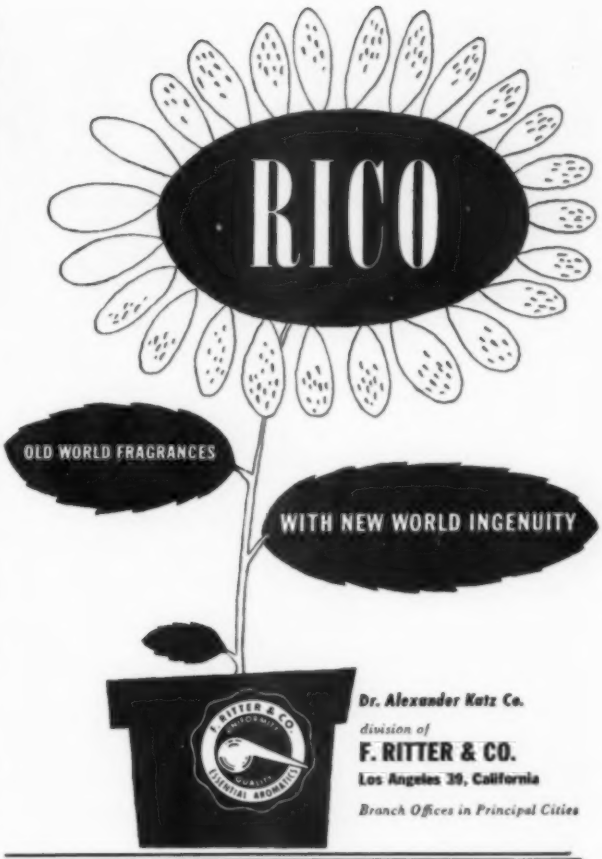
In summarizing the applications of animal testing of chemicals, I should like to emphasize that whether the test subject be animal or human, the test can be no better than the team of investigators conducting it. I strongly feel that the chemical evaluation from the cosmetic standpoint is essentially a teamwork proposition involving cosmetic chemists, pharmacologists, and dermatologists. The most important aspect is a careful delineation of the objective which is being sought and a recognition of the limitations of whatever methods are being applied, whether to animals or to humans. Certainly most species have their place in the overall program. We strongly recommend the use of animals for all of the preliminary screening and evaluation phases. This applies to irritation, sensitization, and preliminary cosmetic aspects. To do otherwise poses an unnecessary hazard to the human test subject and severely limits the scope and volume of the screening which can be completed. In effect, our view is to know the advantages and limitations of each group of subjects and to use the animal wherever the use is practical, since if the cosmetic industry is to make the advances which the progress of chemistry has made available to it, both animal and human resources must be used to the ultimate maximum capacity. There is much work to be done with each species, and each has its place in the overall program.

MODERN TREATMENT OF ACNE

(*Continued from page 616*)

healing stimulant. This cream is rubbed lightly on the face and other acne-involved areas each evening and is easily removed in the morning.

In the presence of pustular eruptions, acne patients may require the administration of sulfa drugs or antibiotics, in addition to other measures.[14] Prevention of pustules is essential to avoid disfiguring scars. For this purpose, Andrews and his associates[9] administer



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sulfadiazine, although in some cystic cases do better with sulfapyridine. In Canada, Hurst[20] reported that in over 90 per cent of his cases, adequate oral concentrations of a triple sulfonamide brought rapid improvement of the pustular element is severe cystic and nodular forms of acne.

Of course, the antibiotics have had extensive trial for the control of the pustular element of acne.[21] As noted by Becker,[16] an effective antibiotic reduces the pustular element and greatly facilitates early improvement. However, relapses are frequent after discontinuance of the antibiotic; making it necessary to repeat the courses. He found that the most effective agents, oxytetracycline (Terramycin) and chlorotetracycline (Aureomycin) produced frequent gastrointestinal upsets.

Kline[11] advises that, in general, antibiotic therapy should not be used routinely. When it is indicated, prolonged therapy with large doses is often necessary. In a similar vein Robinson[22] points out that long-continued administration of these drugs is necessary to obtain and maintain a satisfactory result, hence extreme caution must be observed to avoid serious adverse reactions. In his investigations, penicillin proved to have little beneficial effect, but the broad spectrum antibiotics were of great value in controlling the pustules. He found that oxytetracycline, chlorotetracycline and erythromycin are the drugs of first choice.

Andrews and his colleagues[9] have found that the use of oxytetracycline (Terramycin) has been especially beneficial and well-tolerated in severe pustular types of acne. Other workers[23,24,25] have also reported good results from the use of this antibiotic.

Considerable benefit has likewise been obtained from the use of erythromycin.[26] Van de Erve[27] has recently reported that the trial of erythromycin in 60 cases of acne vulgaris of various types resulted in excellent control of the pustular element in nearly all cases. However this improvement was temporary in nature with recurrence following in the majority of cases within a month after treatment. The drug is apparently safe and is valuable for the control of the pustular phase of acne, but it has little effect on the basic sebaceous overactivity.

Opinion varies with respect to the value of topically applied antibiotics. Kline[11] feels that the local use of these agents is usually of limited value. Going further, Robinson[22] states that the local use of antibiotic therapy is not to be recommended, not only because of the small number of satisfactory responses, but also because of the danger that long continued application may result in acquired contact sensitivity.

Noteworthy, however, are the benefits obtained by Pass and Rattner[28] with a polymyxin B-bacitracin ointment (Polysporin). They used it in treating 577 cases of pyogenic infections of the skin with results that were "altogether satisfactory." There were no toxic reactions or failures in any of these cases, which included 97 patients with pyoderma complicating acne vulgaris.

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Since endocrine dysfunction is considered to be an important causal factor in acne, hormones, notably estrogens, find frequent use in the modern therapy of this condition. As remarked by Payne,[29] most investigators agree that a higher percentage of cures than was formerly obtained is now possible with the employment of estrogens for treating acne. He stresses, however, that estrogens should be used as adjunctive treatment only after older and time-honored etiologic factors have been eliminated. According to Day and Anderson,[15] the indications for the administration of female hormones in acne are: (a) accurate history of menstrual exacerbations, (b) female over 18 years of age with obvious masculine secondary sex characteristics, (c) male or female with severe and intractable acne. They warn that these agents should be employed with caution even where their use is indicated.

Both natural and synthetic estrogenic substances are prescribed in the treatment of acne. Diethylstilbestrol is, of course, the most important of the synthetic estrogens, with a broad background of utility, including the therapy of acne. It is, for example, the first choice of Andrews and his colleagues,[9] who administer it in enteric-coated tablets. Sometimes, this hormone is combined with other agents in capsules for administration to both male and female patients; each capsule containing:

Diethylstilbestrol	0.00025 Gm.
Cascara sagrada, powdered extract	0.01600 Gm.
Thyroid, desiccated	0.00800 Gm.
Sodium bicarbonate	sufficient

During the last year or so, another synthetic estrogenic substance, chlorotrianisene (Tace), has been investigated for its usefulness in treating acne.[30] Welsh[31] treated a group of 151 patients with various types of acne with this hormone; the average duration of therapy being 3.79 months. In this group, 63 patients cleared completely, 87 were controlled satisfactorily, and one patient failed to show any response. From these findings Welsh feels that chlorotrianisene has value for the treatment of acne.

As already indicated, estrogens are also employed for treating acne in males as well as females.[12,29] In the case of the male, however, extra precautions must be observed to avoid undesired reactions, such as breast pain and engorgement. Indeed, Messina[14] feels that oral estrogen medication should be avoided in males, unless the disease is severe. Nonetheless, as noted by Becker,[16] males tolerate small doses of estrogens without untoward reactions, but these agents should be utilized only in the deep-seated eruptions and not before the age of 17, unless other therapy fails and disfigurement is likely to ensue.

Results with estrogens in male patients have been variable. Thus, Andrews and his colleagues[9] found that the administration of diethylstilbestrol to young men with severe oiliness of the skin and acne produced good effects. In contrast, White and Lehmann[32] were disappointed with the results obtained with this hormone and were discouraged from making a wider trial of its use in acne patients.

Estrogens, applied locally in lotions and creams, are also employed in the treatment of acne. Although some opinion[11,33,34] holds that local estrogen therapy is of little or limited value, a number of dermatologists have reported good results from such treatment. Shapiro[35] for example, found that 70 per cent of cases of chronic scarring acne vulgaris, refractory to other forms of therapy, responded favorably to topically applied natural estrogens (Premarin).

The clinical data indicate that male patients benefit more from topical estrogen therapy than do females. Whitelaw,[36] for example, using conjugated estrogenic substances in a nongreasy base (Premarin Cream), found that 55 per cent of his male patients were much improved after treatment for six months or more, while only 21 per cent of the female cases responded satisfactorily. Using the same preparation, Sawicky and his colleagues[37] found that the greatest improvement occurred in the male patients with large cystic lesions.

A lotion (Acnestrol) containing diethylstilbestrol dilaurate was employed by Philip[38] for the local treatment of acne. He reported excellent results in 33 out of 36 male patients. In contrast, only three of 48 females showed improvement.

Combining the old and the new, Lubowe[17] has utilized sulfur-resorcin preparations containing estrogenic hormones such as estrone, estradiol and stilbestrol. He reports that these topical preparations are fairly successful in the adolescent male acne patients, but other adjuvant measures must be employed. About 50 per cent of the patients are favorably affected by the combined regimen. In the female, however, the effectiveness of this local hormone therapy falls to about 15 per cent.

Progesterone, the corpus luteum hormone, has been used in the treatment of acne, with good effect in some cases. According to Day and Anderson,[15] its indications and cautions are essentially the same as for the estrogens; the main objection to its use being the need for parenteral administration. It has been noted[33] that progesterone may be useful in the treatment of acne vulgaris when administered premenstrually. This substance has a beneficial effect on premenstrual tension and through this mechanism may relieve the skin condition.

Newman and Feldman[39] reported that progesterone was effective in preventing or controlling the condition which they have termed "adult premenstrual acne." Administration of the hormone starting about ten days prior to the onset of menstruation was effective in controlling the eruption in the majority of cases. However, Lewis and his associates[40] were disappointed with the results following progesterone administration. In only one of 12 cases could well-defined improvement be attributable to this agent.

Cortisone, which has proved beneficial in the therapy of various dermatologic conditions, has been tried re-

cently in the treatment of acne vulgaris. Didcoct[41] reports that 17 patients, eight males and nine females, were given small doses of this material for periods of ten to 28 days. Evaluation of results on a purely clinical basis revealed that four females and one male showed a mild to moderate suppression of oiliness and a reduction in the number of comedones. This effect was temporary in two females and in the male. Two other females observed a prolonged suppression of comedone and papule formation after stopping cortisone. However, the remaining 12 patients showed no effect from the cortisone.

Alpine or cold quartz lamp irradiations and X-ray therapy are measures that frequently produce good results in acne. The administration ultraviolet rays, says Swartz,[4] is especially indicated when the patient is below par. It also helps to improve the texture of the skin, particularly in instances where there are many comedones and excessive amounts of oil.

In the stubborn and indurated type of acne, says this dermatologist, the X-ray is of great benefit, since it controls the excessive activity of the sebaceous glands. However, he stresses that the administration of such treatment must be carried out by one who understands both the X-ray and the skin.

Significant in this connection is the view held by Andrews and his colleagues[9] regarding this type of therapy, which formerly held a rather high place in acne treatment. They find that their overwhelming success with modern remedies has dulled their desire to use X-rays and this success has whetted their interest in the modern therapeutic approach to acne.

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Hormann & Co., F. R. 714
Horn, John 723
Huisking & Co., Inc., Chas. L. 716

Ising Corp., C. E. 723

Kiefer Machine Co., Karl 666
Kimble Glass ..... Insert facing 624
Kolar Laboratories, Inc. 588
Kolmar Laboratories 598

Lautier Fils 693
Lueders & Co., George 592

Magnus, Mabee & Reynard, Inc. 589
Mallinckrodt Chemical Works ..... Insert facing 609
Maryland Glass Corp. ..... Insert facing 593
Mathieu, Inc., Charles 713
Merck & Co., Inc. 680
Morningstar, Nicol, Inc. 715

National Aniline Div., Allied Chemical & Dye Corp. ..... Insert facing 601
National Association of Private Brand Manufacturers, Inc. 723
New Jersey Machine Corp. 668
New Jersey Zinc Co. 707
New York Quinine & Chemical Works, Inc. 683
Norda Essential Oil & Chemical ..... Cover 2
Nysco Laboratories, Inc. 723

Old Empire Mfg. Chemists, Inc. 713
Onyx Oil & Chemical Company 599
Orbis Products Corp. 674
Owens-Illinois 634, 640

Parsons-Plymouth, Inc., M. W. 708
Pennsylvania Glass Products Co., Inc. 645
Perl Machine Mfg. Co. 716
Pfaltz & Bauer Co., Inc. 721
Pfizer & Co., Inc., Chas. ..... Insert facing 608
Plastic Assembled Products 671
Plax Corporation ..... Insert facing 625
Pneumatic Scale Corp., Ltd. 662
Polak & Schwarz, Inc. 590
Popper & Sons, Inc. 717
Potdevin Machine Co. 715
Private Label Cosmetics 703
Progressive Labelling Machine Inc. 723

Reheis Co., Inc. 705
Risdon Mfg. Co., The 647
F. Ritter & Company 717
Roure-Dupont, Inc. 685

Santonin Company of America 716
Scoville Manufacturing Company ..... Insert bet. 624-625
Sheffield Tube Corp. ..... Insert facing 633
Shulton, Inc. ..... Insert facing 649
Sindar Corporation 654
Standard Pharmacal Co. 719
Sterwin Chemicals, Inc. 579
Stokes Machine Co., F. J. 660
Stokes & Smith Company 670
Strong Cobb & Co., Inc. 606
Sunkist Growers 690
Swift & Co. 595
Synfleur Scientific Labs. 591

Tablet Coating Book 710
Tamms Industries, Inc. 721
Trade Mark Record Book 718

Ungerer & Co., Inc. ..... Cover 3
Union Carbide & Carbon Corp., Carbide & Carbon Chemicals Div. 650
U. S. Bottlers Machine Co. 709

van Ameringen-Haebler, Inc. ..... Insert bet. 592-593; Pg. 604
Vanderbilt Co., R. T. 702
Van Dyk & Company, Inc. 597
Verona Chemical Co. ..... Insert facing 656
Vitamerican Oil Corp. 712

Welch, Holme & Clarke, Inc. 704
Wheaton Co., T. C. ..... Insert facing 632
Will & Baumer Candle Co. 672
Wolf & Co., Jacques 711

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